



REVIEW

Essential Oils in Oral Squamous Cell Carcinoma: From Plant Ecology to Antitumoral Mechanisms

Bianca Voicu Balasea¹, Melis Izet¹, Florentina Rus², Cristina Neculau^{1,*}, Alexandra Popa^{2,*}, Ana Cernega³, Alexandra Ripszky^{1,2,#} and Simona Parvu^{4,5,#}

¹The Interdisciplinary Center for Dental Research and Development, “Carol Davila” University of Medicine and Pharmacy, 19-21 Jean Louis Calderon, Bucharest, Romania

²Department of Biochemistry, Faculty of Dental Medicine, “Carol Davila” University of Medicine and Pharmacy, 17-23 Plevnei Street, Bucharest, Romania

³Department of Professional Organization and Medical Legislation-Malpractice, “Carol Davila” University of Medicine and Pharmacy, 37 Dionisie Lupu Street, Bucharest, Romania

⁴Department of Hygiene, Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, 37 Dionisie Lupu, Bucharest, Romania

⁵National Institute of Public Health, Bucharest, Romania

*Corresponding Authors: Cristina Neculau. Email: cristina.neculau@drd.umfcd.ro;

Alexandra Popa. Email: alexandra.popa@umfcd.ro

#These authors contributed equally to this work

Received: 10 July 2026; Accepted: 16 September 2026; Published: 19 October 2026

ABSTRACT: Plant-derived essential oils (EOs) are complex mixtures of secondary metabolites that play pivotal ecological roles in plants, including defense against herbivores, pathogens, and abiotic stress, as well as signaling in plant-environment interactions. These metabolites exhibit chemical diversity, often correlated with plant taxonomy, organ-specific accumulation (e.g., leaves, flowers, rhizomes), and geographical distribution. This review summarizes plants producing EOs with antitumor activity in oral squamous cell carcinoma (OSCC) models, linking taxonomy, organ-specific accumulation, and ecological roles with observed biological effects. Several phylogenetically diverse plant families, including Lamiaceae, Lauraceae, Piperaceae, Zingiberaceae, Apiaceae, Asteraceae, Scrophulariaceae, and Cupressaceae, produce EOs whose major constituents—thymol, carvacrol, eugenol, cinnamaldehyde, α -pinene, β -pinene, and zerumbone—predominantly exhibit antiproliferative and pro-apoptotic activities in OSCC models, with several species also showing anti-migratory effects and modulation of cell-cycle progression, oxidative stress, and cancer-related signaling pathways. These bioactivities may reflect, at least in part, biochemical properties originally evolved for plant defense and adaptation to biotic and abiotic stress, highlighting a conceptual connection between ecological function and antitumoral activity in OSCC that requires further experimental validation. Future studies should focus on standardization of essential oil composition, mechanistic validation, and well-designed preclinical and clinical investigations to facilitate the development of essential oil-derived compounds as complementary therapeutic strategies for OSCC.

KEYWORDS: Essential oils; oral squamous cell carcinoma; ecological role; anticancer activity

1 Introduction

Essential oils are biosynthesized by aromatic plants and are typically accumulated in specialized secretory structures, particularly glandular trichomes, as well as other secretory tissues located in leaves,

flowers, stems, and underground organs [1]. Their chemical composition is predominantly represented by mono- and sesquiterpenes and phenylpropanoids [2]. The qualitative and quantitative variability of these metabolites is closely linked to genetic background, environmental conditions, and ecological interactions, resulting in substantial chemotypic variability among species and populations [2,3].

From a botanical and ecological perspective, essential oils function as multifunctional secondary metabolites that mediate plant–environment interactions. They contribute to plant defense against herbivores and pathogens by mediating direct and indirect protective mechanisms, including interactions with natural enemies of herbivores and neighboring plants, while also participating in signaling processes associated with biotic and abiotic stress responses [4]. In addition, essential oils are increasingly recognized for their involvement in plant adaptation to environmental constraints, particularly drought and salinity, through a range of physiological, biochemical, and molecular mechanisms that enhance stress tolerance and resilience [5]. These functions support the view that essential oils may act as evolutionarily shaped chemical systems contributing to plant fitness under diverse environmental pressures.

In this context, plant-derived essential oils (EOs) have attracted increasing scientific attention in oncology due to their complex composition of volatile secondary metabolites with reported antimicrobial, antioxidant, anti-inflammatory, and anticancer properties [6,7].

In oral oncology, essential oils and their constituents have been widely investigated in oral squamous cell carcinoma (OSCC). OSCC remains the most common malignancy of the oral cavity and a major global health burden [8]. Increasing experimental evidence indicates that several essential oil constituents exert significant cytotoxic and antiproliferative effects in OSCC models, primarily through the induction of apoptosis [9,10]. Additional mechanisms, including modulation of oxidative stress, cell-cycle regulation, and oncogenic signaling pathways, have also been reported [11].

Therefore, this review aims to systematically analyze medicinal and aromatic plants producing essential oils from a combined botanical and ecological perspective, focusing on their taxonomic classification, geographical distribution, organ-specific accumulation of volatile compounds, and ecological roles. Furthermore, it seeks to correlate these characteristics with their reported antitumoral activity in OSCC models, thereby providing an integrated perspective that bridges plant chemical ecology with experimental oral oncology.

2 Botanical and Ecological Characterization of Medicinal Plants Producing Antitumoral Essential Oils

The following medicinal plants produce essential oils with reported antitumoral effects in OSCC: *Thymus* spp. [12,13], *Cinnamomum* spp. [14], *Piper rivinoides* [15,16], *Zingiber zerumbet* [17], *Levisticum officinale* [18], *Spilanthes paniculata* [19], *Scrophularia oxysepala* [20], *Salvia officinalis* [13], *Mentha piperita* [13], *Juniperus communis* [13], and *Rosmarinus officinalis* [13].

2.1 *Thymus* sp.

2.1.1 Taxonomy

Thymus is a genus of the Lamiaceae (Labiatae) family, which comprises more than 200 genera. The genus includes approximately 215 accepted species, among which *Thymus vulgaris* L., commonly known as garden thyme, is the most widely used species and the principal representative of the genus in commercial applications [21].

2.1.2 Geographical Distribution

The genus *Thymus* is widely distributed throughout Eurasia, extending also into Africa and southern Greenland. In Bulgaria, the genus is represented by 21 species belonging to the sections *Hyphodromi* and *Serpyllum*, six of which are endemic to the Balkan Peninsula [22]. Thymol and carvacrol, among the principal bioactive constituents reported across *Thymus* species, have been associated with a broad range of documented health-related properties [23]. *Thymus vulgaris* L. is native to the Western Mediterranean region, with its natural distribution extending from Spain and the Balearic Islands to south-eastern Italy, including southern France and Greece [21,24]. The species occurs across a wide altitudinal range and has been reported at elevations reaching 1600 m in the Italian Alps and up to 2000 m in Spain [24]. Spain is the leading producer of thyme essential oil, accounting for the majority of global production. In addition, *T. vulgaris* is cultivated in several European countries, including France, Germany, Switzerland, Portugal, Italy, Bulgaria, Hungary, Turkey and Greece, as well as in regions of North America, North Africa, Asia, South America, Oceania and the Middle East [21].

2.1.3 Essential Oil-Accumulating Organs

The essential oil of *Thymus vulgaris* is primarily accumulated in the aerial parts of the plant, particularly in the leaves and flowering tops, which are the main organs used for essential oil extraction. The synthesis and storage of the essential oil take place in specialized secretory structures known as glandular trichomes, which are distributed on the surface of these plant organs [21].

2.1.4 Ecological Role of *Thymus vulgaris* Essential Oil

Volatile compounds produced by *Thymus* species play an important role in plant defense and ecological interactions. In *Thymus vulgaris*, these compounds contribute to protection against pathogens, herbivores, and insects, while also attracting pollinators, particularly bees, which are essential for cross-pollination [21]. The defensive function of thyme essential oil has been demonstrated against insect pests. *Thymus vulgaris* essential oil reduced survival, longevity, oviposition, and adult emergence of the bean weevil (*Acanthoscelides obtectus*), suggesting its potential as a natural botanical insecticide [25]. Similarly, thymol and carvacrol exhibit insecticidal activity against various insect species, including *Musca domestica*, further supporting their ecological role in plant defense [26]. In addition, *Thymus* essential oils display strong antimicrobial activity, particularly against *Candida* species. Among the studied species, *Thymus pulegioides* and *Thymus serpyllum* showed the highest antimicrobial efficacy, likely due to synergistic interactions among their volatile constituents [24].

Thymus vulgaris essential oil has also demonstrated direct antimicrobial efficacy against phytopathogenic bacteria and fungi, including *Pseudomonas syringae*, *Xanthomonas hortorum*, *Erwinia carotovora*, *Fusarium culmorum*, *Alternaria alternata*, *Botrytis cinerea*, and *Pythium debaryanum*, supporting its ecological role as a direct defense agent against organisms that naturally threaten plant health [27]. According to Vassiliou et al. [28], this antimicrobial activity is mainly attributed to thymol and carvacrol, which disrupt microbial cell membrane integrity. Carvacrol acts rapidly, damaging the cell membrane, altering its morphology, increasing permeability, and causing cytoplasmic leakage that leads to cell death. Thymol instead inhibits microbial growth by inducing autolysis, suppressing biofilm formation, and blocking cellular proliferation; in fungi, it also targets ergosterol, compromising membrane structure and function. Carvacrol further contributes to the antifungal effect by lowering extracellular pH, damaging membranes, and reducing cellular lipid content [28].

2.2 *Cinnamomum* spp.

2.2.1 Taxonomy

The genus *Cinnamomum* belongs to the family Lauraceae and comprises approximately 336 species of evergreen aromatic trees and shrubs [29]. Traditionally classified within the tribe *Cinnamomeae*, the genus has undergone substantial taxonomic revision following recent phylogenetic studies. Molecular evidence has demonstrated that *Cinnamomum* is diphyletic, supporting its separation into the distinct genera *Cinnamomum* and *Camphora* [30]. Among the numerous cinnamon species recognized worldwide, *Cinnamomum cassia* and *Cinnamomum verum* are the most extensively cultivated and commercially important representatives of the genus [31].

2.2.2 Geographical Distribution

Species of the genus *Cinnamomum* are widely distributed across tropical and subtropical regions, with major cultivation areas located in China, India, Madagascar, and Sri Lanka [31]. Among them, *Cinnamomum verum* J. Presl. (syn. *C. zeylanicum* Blume), commonly known as true or Ceylon cinnamon, is native to Sri Lanka and southern India. Its distribution has expanded to several other regions, including Southeast Asia, China, Myanmar, Indonesia, Madagascar, the Caribbean, Australia, and Africa [29].

China is the leading producer of cinnamon essential oil worldwide, accounting for nearly 80% of global production. In this country, *C. cassia* represents the predominant cultivated species and is mainly grown in the provinces of Guangdong and Guangxi, where the variety known as “Xijiang Cinnamon” is extensively cultivated [31].

2.2.3 Essential Oil-Accumulating Organs

Cinnamon essential oil (CEO) is obtained primarily from the bark and leaves of *Cinnamomum* spp. The bark, corresponding to the secondary phloem, is characterized by a higher density of oil cells and resinous structures compared to leaf tissues, resulting in greater essential oil accumulation. Consequently, bark represents the main source of CEO, although its regeneration rate is lower than that of leaves. In addition to its role in essential oil production, cinnamon bark is also directly utilized as a culinary spice [31].

2.2.4 Ecological Role of *Cinnamomum* spp. Essential Oil

In vitro studies have demonstrated that cinnamon bark essential oil inhibits the growth of a wide range of fungal and bacterial species, including direct activity against phytopathogens such as *Dickeya dadantii*, *Pectobacterium carotovorum*, *Pseudomonas syringae*, *Xanthomonas hortorum*, *Fusarium graminearum*, *Rhizoctonia solani*, and *Phytophthora cinnamomi*, highlighting its potential as a natural fungicidal and bacteriostatic agent and reinforcing its ecological function in protecting plant tissues against natural microbial threats [32].

Its major constituent, cinnamaldehyde, exhibits strong antimicrobial activity against Gram-positive bacteria such as *Staphylococcus aureus* and Gram-negative bacteria including *Salmonella* spp., *Escherichia coli*, and *Pseudomonas aeruginosa*, as well as antifungal effects against *Candida albicans*, *Aspergillus niger*, and *Cryptococcus neoformans* [33].

The antimicrobial activity of cinnamon essential oil is associated with membrane disruption, interference with enzymatic systems, and modulation of cellular redox balance, making it a promising candidate for sustainable plant protection strategies [32]. Consistent with these findings, cinnamon oil has been

proposed as a natural alternative to synthetic pesticides due to its antimicrobial, antifungal, and insecticidal properties, including activity against insect pests and fungal pathogens such as grey mould [34].

In addition to its direct antimicrobial effects, cinnamon essential oil may enhance plant defense responses through the activation of systemic acquired resistance (SAR) and induced systemic resistance (ISR), promoting the synthesis of phytoalexins, lignin, and other defense-related metabolites [32]. Collectively, these findings suggest that cinnamon essential oil plays an important ecological role by protecting plant tissues against microbial pathogens and insect pests while enhancing resistance to environmental stressors.

The antimicrobial activity of cinnamon essential oil is mainly attributed to cinnamaldehyde, which interferes with cellular processes and disrupts membrane function, leading to inhibition of pathogen growth and eventual cell death, while eugenol further enhances these antimicrobial and antifungal effects [34]. More broadly, *Cinnamomum* spp. essential oil displays a multitarget mode of action, involving disruption of membrane integrity, interference with enzymatic and metabolic processes, and perturbation of cellular redox balance; the persistent post-exposure inhibition observed in some fungal pathogens further suggests long-lasting cellular damage and both fungistatic and fungicidal activity [32].

2.3 *Piper Rivinoides*

2.3.1 Taxonomy

The genus *Piper* (family Piperaceae) is placed within the order Piperales and belongs to the Magnoliids clade of angiosperms, which is considered part of the basal lineages of flowering plants. Phylogenetic analyses support the monophyly of the genus and recognize approximately 2000 species worldwide [35]. Within the Neotropical region, eight subgenera have been described, including *Enckea*, *Macrostachys*, *Ottonia*, *Peltobryon*, *Piper*, *Pothomorphe*, *Radula*, and *Schilleria* [35]. Representative species include *Piper aduncum* L., *P. betle* L., *P. multinodum* C. DC., and *P. rivinoides* Kunth [36].

2.3.2 Geographical Distribution

Piper L. is a pantropically distributed genus, occurring throughout tropical regions across the globe. Within the Neotropical zone, its distribution spans from northern Mexico through Central and South America, reaching as far as Chile and Argentina. The highest levels of species diversity are concentrated in the Andean regions, Central American lowlands, and Central Amazonia, which are considered major diversity hotspots for the genus [35]. At the species level, *Piper rivinoides* Kunth is indigenous to Brazil, where it forms part of the native flora [36].

2.3.3 Essential Oil-Accumulating Organs

In *Piper rivinoides*, the leaves represent the main essential oil-accumulating organ, exhibiting the highest oil yield compared to roots, stems, and branches [37].

2.3.4 Ecological Role of *Piper rivinoides* Essential Oil

Essential oils from *Piper* species exhibit a broad spectrum of biological activities that may contribute to plant defense against biotic stressors. Felisberto et al. [36] reported an organ-specific distribution of volatile metabolites in *Piper rivinoides*, with leaves accumulating higher levels of α -pinene and β -pinene, compounds commonly associated with protection against herbivores, pathogens, and abiotic stress factors. In contrast, roots contained higher concentrations of apiole, suggesting a potential role in belowground defense against soil-associated microorganisms and other biotic interactions.

The antimicrobial properties of *Piper* essential oils further support their ecological significance. Essential oils from several species have shown activity against Gram-positive bacteria, including *Staphylococcus aureus*, *Bacillus cereus*, *Bacillus subtilis*, and *Streptococcus pyogenes*, as well as Gram-negative bacteria such as *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* [35]. Additionally, the leaf essential oil of *P. diospyrifolium* demonstrated antifungal activity against *Candida albicans*, *Candida parapsilosis*, and *Candida tropicalis* [35].

Piper rivinoides has also been identified as promising sources of compounds with antimycobacterial potential [36]. Together, these findings suggest that *Piper* essential oils contribute to the plant's chemical defense system by protecting tissues against microbial pathogens and other biological threats, thereby enhancing resistance to environmental stress.

2.4 Zingiber Zerumbet

2.4.1 Taxonomy

The family Zingiberaceae comprises rhizomatous monocotyledonous plants and represents a large taxonomic group with approximately 52 genera and around 1400 species. Within this family, the genus *Zingiber* includes several medicinal and ornamental species of economic importance, such as *Zingiber montanum* and *Zingiber zerumbet* [38,39]. *Zingiber zerumbet* (L.) Roscoe ex Sm. is closely related to *Zingiber officinale* and is known by various common names, including bitter ginger, wild ginger, and shampoo ginger, the latter reflecting the traditional use of its inflorescence as a natural surfactant source [40].

2.4.2 Geographical Distribution

Zingiber zerumbet is native to Southeast Asia and is widely distributed throughout tropical and subtropical regions. Its natural range includes countries such as India, Bangladesh, Malaysia, Nepal, and Sri Lanka, although long-term cultivation has expanded its presence across many other tropical areas worldwide [38]. The species is commonly found in humid, shaded habitats, often growing near rivers and waterfalls.

It also occurs naturally in the Himalaya and the Western Ghats of India, where it grows as an aromatic and rhizomatous herb [41]. Today, it is also cultivated in other tropical regions, including parts of South America such as rural areas of Brazil [40].

2.4.3 Essential Oil-Accumulating Organs

In *Zingiber zerumbet*, essential oil accumulation differs between plant organs. The rhizomes constitute the main reservoir, exhibiting a markedly higher essential oil content compared to the aerial parts. Leaves, stems, and inflorescences also contain essential oil, but in lower quantities relative to the rhizome [38].

2.4.4 Ecological Role of *Zingiber zerumbet* Essential Oil

Essential oils extracted from *Zingiber zerumbet* rhizomes exhibit multiple biological activities, including antimicrobial and antimalarial activity [41]. The major bioactive compound identified in the essential oil is zerumbone, which has been linked to antibacterial activity [42]. Zerumbone has shown broad antimicrobial effects against both Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli* and *Helicobacter pylori* [42]. Furthermore, the rhizome essential oil and its principal constituent have been reported to possess antimalarial, antimicrobial and antiviral properties [38]. Together, these activities suggest that volatile compounds, particularly zerumbone, contribute to the plant's chemical defense system by protecting rhizomes against microbial pathogens and

insect pests, thereby enhancing resistance to biotic stress. The antimicrobial activity of *Zingiber* essential oil is primarily associated with disruption of microbial cell membranes: the oil compromises membrane integrity and increases permeability, causing leakage of intracellular components such as proteins, nucleic acids, and ATP, which impairs essential cellular functions and ultimately leads to microbial cell death [43].

2.5 *Levisticum Officinale*

2.5.1 Taxonomy

Lovage (*Levisticum officinale* Koch) is a member of the Apiaceae family, one of the largest angiosperm families. Species within Apiaceae are commonly characterized by aromatic or pungent properties, which are mainly associated with the presence of essential oils. The family includes numerous species with culinary and medicinal importance [44].

2.5.2 Geographical Distribution

According to Olennikov et al. [45], *Levisticum officinale* is native to Southwestern Asia, particularly the Hazaran Mountains in the Kerman province of Iran, as well as parts of Southern Europe. From its native range, the species has been widely cultivated and introduced worldwide, especially across temperate regions, where it is now commonly grown as a culinary and medicinal plant [45].

2.5.3 Essential Oil-Accumulating Organs

The main organ of essential oil accumulation in *Levisticum officinale* is the root, which has been extensively investigated as a rich source of volatile compounds, particularly phthalides (e.g., ligustilide and its derivatives), as well as mono- and sesquiterpenes [45]. However, essential oils are also present in other plant organs, including leaves, stems, fruits, and flowers. The leaves contain terpene-rich essential oils and have demonstrated significant biological activity, including hepatoprotective effects through the reduction of oxidative stress [46]. Fruits and flowers also accumulate volatile constituents, while stems contain similar compounds to those found in other aerial parts, although they have been less extensively studied. Overall, roots are considered the primary site of essential oil accumulation in *L. officinale* [45].

2.5.4 Ecological Role of *Levisticum officinale* Essential Oil

The ecological role of bioactive constituents in *Levisticum officinale* appears to be closely related to plant defense and environmental adaptation. Phenolic acids, flavonoids, and tannins contribute to protection against both biotic and abiotic stresses through antimicrobial, antioxidant, and structural defense mechanisms. Flavonoids are particularly abundant in leaves, where they are involved in protection against UV radiation and pathogen attack, reflecting the direct exposure of aerial organs to environmental stressors. In contrast, the accumulation of phenolic compounds in roots has been associated with defense against soil microorganisms and other subterranean stress factors. Phenolic acids such as caffeic, ferulic, and chlorogenic acids further enhance plant resistance by inhibiting pathogenic microorganisms and strengthening cell wall structure. Condensed tannins also play an important ecological role as defense agents against herbivores and pathogens, being concentrated in exposed organs such as leaves. Overall, the organ-specific distribution of these metabolites suggests a functional adaptation strategy, whereby leaves are primarily protected against above-ground environmental challenges, while roots are specialized for protection against soil-borne threats and support plant survival under stressful conditions [47].

The antimicrobial activity of *Levisticum officinale* essential oil against multidrug-resistant *Mycobacterium tuberculosis* appears to be related to inhibition of 2-trans-enoyl-acyl carrier protein reductase (InhA),

a key enzyme in mycobacterial cell wall biosynthesis. Molecular docking analyses showed that the oil's major constituents, including α -terpinyl acetate, neocnidilide, β -phellandrene, and (Z)-ligustilide, bind with affinities comparable to or higher than isoniazid, suggesting they interfere with cell wall formation and thereby inhibit bacterial growth [48].

2.6 *Spilanthes Paniculata*

2.6.1 Taxonomy

The genus *Spilanthes* Jacq. belongs to the family Asteraceae and is classified within the subtribe Verbesininae of the tribe Anthemideae. It comprises more than 300 species. In India, the genus is represented by six species, including *Spilanthes calva*, *S. paniculata*, *S. radicans*, *S. ciliata*, *S. uliginosa*, and *S. oleracea* [19,49].

However, taxonomic revisions have shown that several species previously assigned to *Spilanthes*, including *S. paniculata*, are currently reclassified under the genus *Acmella*. This reclassification is important for the correct interpretation of ethnobotanical and phytochemical studies, where historical nomenclature may differ from the updated taxonomy [50].

2.6.2 Geographical Distribution

The genus *Spilanthes* is widely distributed in tropical and subtropical regions. Its occurrence spans several areas of Asia, Africa, and the Americas, including countries such as Sri Lanka, India, Borneo, North Australia, Malaysia, and various tropical regions of Africa and America [49].

2.6.3 Essential Oil-Accumulating Organs

In *Spilanthes paniculata*, essential oil is mainly concentrated in the flowers and leaves, which are the primary plant parts used for extraction, with flowers exhibiting the highest yield and chemical diversity, while stems and roots contain comparatively lower amounts [19,51].

2.6.4 Ecological Role of *Spilanthes paniculata* Essential Oil

Studies on *Spilanthes* species indicate that volatile compounds contribute to plant defense against a range of biotic stressors. Extracts have shown antifungal activity against species such as *Aspergillus* and *Fusarium*, with inhibition increasing in a dose-dependent manner [51,52]. In addition, spilanthal and related constituents exhibit strong larvicidal and insecticidal effects, affecting developmental stages and survival of various insect species through neurophysiological disruption and mortality [52,53]. These effects suggest that volatile and bioactive compounds in *Spilanthes* function as chemical defenses, reducing fungal colonization and limiting damage from insect herbivores and disease vectors, thereby enhancing plant survival in natural environments.

The essential oil of *Spilanthes paniculata* exhibited significant antibacterial activity against both Gram-positive and Gram-negative bacteria. Zhu et al. suggest that this activity is related to the hydrophobic nature of the oil, which is rich in sesquiterpene hydrocarbons and other terpenoid compounds. These constituents are thought to interact with microbial cell membranes, thereby inhibiting pathogen growth. Gram-positive bacteria were generally more susceptible than Gram-negative bacteria, likely due to the protective hydrophilic outer membrane present in Gram-negative species, which limits the penetration of hydrophobic essential oil components [54].

2.7 *Scrophularia Oxysepala*

2.7.1 Taxonomy

The genus *Scrophularia* L. (1753) belongs to the family Scrophulariaceae Juss. within the order Lamiales. It represents the type genus of the family and includes approximately 250 species, predominantly consisting of herbaceous or suffrutescent perennial plants [55].

2.7.2 Geographical Distribution

Scrophularia oxysepala is distributed within the Iran–Turanian floristic region, which represents the main center of diversity for the genus *Scrophularia*. Available floristic and herbarium data indicate that the species occurs mainly in Iran and adjacent areas of Southwest Asia, where it is associated with montane and submontane habitats. It typically grows on rocky slopes, steppe margins, and dry valleys under xeric conditions. Its distribution is relatively restricted and patchy, reflecting the fragmented nature of suitable habitats in mountainous landscapes of the region [56].

2.7.3 Essential Oil-Accumulating Organs

The essential oil of *Scrophularia oxysepala* is primarily accumulated in the aerial parts of the plant, with leaves representing the main organ used for extraction [20].

2.7.4 Ecological Role of *Scrophularia oxysepala* Essential Oil

Studies on *Scrophularia oxysepala* indicate that its secondary metabolites, particularly iridoid glycosides and phenylpropanoid derivatives, play an important role in plant defense against biotic stressors. Methanolic extracts and enriched fractions have demonstrated notable free radical scavenging activity, suggesting a protective function against oxidative stress induced by environmental factors. In addition, specific fractions rich in acylated iridoids exhibited significant insecticidal effects against *Oryzaephilus mercator*, indicating a role in reducing herbivore pressure through contact toxicity and deterrence of insect feeding. Furthermore, the extracts showed antimalarial activity via inhibition of heme biocrystallization, reflecting broader bioactivity against eukaryotic pathogens and supporting a defensive chemical potential [57]. Overall, these findings suggest that the bioactive compounds in *S. oxysepala* function as multifunctional chemical defenses that contribute to protection against insect herbivory and oxidative stress, thereby enhancing plant fitness and ecological adaptation in its native habitats.

2.8 *Salvia Officinalis*

2.8.1 Taxonomy

The genus *Salvia* L. belongs to the family Lamiaceae, subfamily Nepetoideae, and represents one of the largest genera in the plant kingdom, comprising approximately 1000 species. Within this genus, several species, including *Salvia officinalis*, *S. apiana*, *S. divinorum*, *S. fruticosa*, and *Salvia rosmarinus*, are of significant ethnobotanical and cultural importance worldwide [58,59]. *Salvia officinalis* L. is an aromatic herb belonging to this genus and is widely recognized for its medicinal and culinary relevance [59].

2.8.2 Geographical Distribution

The genus *Salvia* L. is widely distributed worldwide, comprising approximately 1000 species with a broad geographical range across multiple continents [60]. Ethnopharmacological evidence reports the

use of around 187 *Salvia* species across Asia, Europe, Africa, and the Americas, reflecting the extensive distribution and diversity of the genus [58].

Salvia officinalis L. is native to the northern Mediterranean Basin, with its main distribution centered in the Balkan Peninsula, extending from the Gulf of Trieste to central Greece, and with smaller populations occurring in the central and southern Apennines of Italy. The species is typically associated with calcareous habitats in the Adriatic region, and its principal center of genetic diversity is located within the central Balkans, which is also considered a key area for its phylogeographic structure [61].

2.8.3 Essential Oil-Accumulating Organs

The essential oil of *Salvia officinalis* is accumulated in the aerial parts of the plant, particularly in the leaves and stems. Within these organs, essential oil is stored in specialized epidermal secretory structures, mainly glandular trichomes. These trichomes consist of a short stalk and a multicellular head covered by a cuticle, beneath which the secreted oil accumulates in a subcuticular space [62].

In addition to glandular trichomes, other secretory structures such as cavities and channels may also contribute to essential oil storage, with trichome density being positively correlated with essential oil yield [62].

2.8.4 Ecological Role of *Salvia officinalis* Essential Oil

The essential oil of *Salvia officinalis* is rich in volatile terpenoid compounds such as α -thujone, β -thujone, camphor, and 1,8-cineole, which collectively contribute to its ecological functions in plant defense and environmental adaptation. These constituents exhibit strong antimicrobial activity against bacterial and fungal pathogens, including *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans*, highlighting their role in protecting the plant from phytopathogens [63]. In addition, sage essential oil demonstrates insecticidal effects against pests such as *Spodoptera littoralis* larvae and *Tribolium castaneum* adults, as well as allelopathic activity that inhibits seed germination and seedling growth of competing plants, indicating its broader role in interspecific competition and herbivore deterrence [64]. Beyond biotic stress protection, these volatile compounds also contribute to abiotic stress tolerance, as their production increases under moderate drought conditions, suggesting that essential oil biosynthesis is integrated into the plant's physiological response to water deficit [65]. Drought stress influences both essential oil composition and yield, with moderate stress enhancing oil accumulation while severe stress reduces overall biomass, reflecting a trade-off between growth and secondary metabolite production [65]. Furthermore, minor constituents such as linalool and other terpenes contribute to antioxidant activity, potentially mitigating oxidative stress under harsh Mediterranean environmental conditions [63]. Overall, *S. officinalis* essential oil functions as a multifunctional chemical defense system, enhancing resistance against pathogens, herbivores, and competing plants while also contributing to stress adaptation and ecological fitness under variable environmental conditions.

The antipathogenic activity of *Salvia officinalis* essential oil is associated with the presence of terpenic and terpenoid compounds, such as camphor, thujone, and 1,8-cineole, which exert bactericidal and bacteriostatic effects through the inhibition of pathogenic microorganism growth. In addition, the essential oil exhibits antifungal and antiviral activity, these effects being attributed to bioactive constituents of the plant, including diterpenes with antiviral activity [66].

2.9 *Mentha piperita*

2.9.1 Taxonomy

The genus *Mentha* L. belongs to the family Lamiaceae and is characterized by high taxonomic complexity due to extensive morphological variability and hybridization. Taxonomic studies have recognized multiple species and hybrids within the genus, including *Mentha aquatica*, *M. spicata*, *M. arvensis*, *M. longifolia*, *M. rotundifolia*, *M. pulegium*, as well as several hybrid taxa such as *M. × piperita*, *M. × villosa*, *M. × verticillata*, *M. × gentilis*, and *M. × gracilis* [67]. Among these, *Mentha piperita* L. (peppermint) is a widely studied hybrid species resulting from the cross between *Mentha aquatica* L. and *Mentha spicata* L. [68].

2.9.2 Geographical Distribution

Mentha piperita is native to Europe, but it is now widely cultivated and naturalized in many regions worldwide. Its cultivation extends across North America (including the United States and Canada), Asia, North Africa, and other temperate and subtropical areas, reflecting its broad adaptability and global economic importance [68].

2.9.3 Essential Oil-Accumulating Organs

In *Mentha piperita*, the essential oil is accumulated primarily in the aerial parts of the plant, with leaves representing the main organ of storage. Within the leaves, essential oil is synthesized and stored in peltate glandular trichomes located on the leaf surface, which constitute the principal sites of monoterpene production and accumulation. In contrast, the stem plays a minor role in essential oil biosynthesis and storage, as these processes are predominantly associated with leaf tissues [68,69].

2.9.4 Ecological Role of *Mentha piperita* Essential Oil

EOs produced by *Mentha* species are complex mixtures of volatile secondary metabolites, predominantly monoterpenes such as menthol, menthone, carvone, limonene, and pulegone. Although these compounds are not directly involved in primary metabolism, they play important ecological roles by mediating interactions between plants and their environment [68,70].

One of the principal ecological functions of *Mentha* EOs is chemical defense against herbivores and pathogens. Monoterpenes can act as deterrents or toxic compounds, reducing insect feeding and inhibiting the growth of pathogenic microorganisms. The defensive role of these metabolites is further supported by the observation that jasmonate signaling, a key pathway activated during biotic stress, enhances both glandular trichome development and monoterpene biosynthesis [70]. Moreover, the documented activity of *Mentha* EOs against aphids, termites, fungi, and plant pathogens is consistent with their protective role in plants [68].

In addition to defense, volatile monoterpenes participate in plant–insect interactions, including pollinator attraction and herbivore defense [68,70]. These ecological functions may contribute to plant fitness and adaptation in natural environments.

The ecological role of *Mentha* EOs is closely linked to their chemical plasticity. Environmental factors such as temperature, light intensity, water availability, soil characteristics, and developmental stage significantly influence EO yield and composition [71]. Such variability suggests that essential oil production may represent an adaptive mechanism that enables *Mentha* species to respond to changing environmental conditions and stress factors.

Overall, available evidence indicates that *Mentha* essential oils function as multifunctional mediators of ecological interactions involved in defense, communication, and environmental adaptation. Their diverse biological activities and environmentally responsive biosynthesis help explain the remarkable chemical diversity observed within the genus *Mentha*.

The essential oil of *Mentha piperita* exhibits antipathogenic activity through the antimicrobial effects of its bioactive constituents, particularly menthol and other monoterpenes, which contribute to the inhibition of bacterial and fungal growth. Its activity is demonstrated by the higher susceptibility of Gram-positive bacteria compared with Gram-negative species, a difference attributed to the specific characteristics of the bacterial cell envelope. Moreover, *M. piperita* essential oil can interfere with microbial biofilm formation, including through the inhibition of glycosyltransferase genes involved in the synthesis of extracellular polymers, thereby reducing bacterial adhesion and colonization. These antimicrobial effects, together with the reported antioxidant and anti-inflammatory properties, support the potential use of *M. piperita* essential oil as a complementary agent for controlling microbial infections [68].

2.10 *Juniperus Communis*

2.10.1 Taxonomy

The genus *Juniperus* L. belongs to the family Cupressaceae and represents one of the most polymorphic genera within the order Cupressales. It comprises approximately 75 species of evergreen aromatic shrubs and trees distributed worldwide. Within this genus, several well-known species include *Juniperus communis*, *Juniperus recurva*, and *Juniperus indica*, which are reported from regions such as the western Himalayan area of India [72,73].

2.10.2 Geographical Distribution

The genus *Juniperus* is widely distributed across the Northern Hemisphere, occurring in temperate, montane, and arid regions of Europe, Asia, and North America, with additional occurrences on several oceanic islands. Its diversity is structured around two major centers, the Mediterranean Basin, considered the primary diversification hotspot, and the East Asian (Sino-Japanese) region, which are biogeographically linked through historical floristic connections [74].

Within its range, *Juniperus* species are also extensively distributed in the temperate Himalaya, extending from Kashmir to Bhutan and western Tibet, at elevations between 2500 and 4700 m [72]. Long-distance dispersal events have further contributed to the presence of the genus on Macaronesian islands, including the Azores, Canary Islands, and Madeira [74].

2.10.3 Essential Oil-Accumulating Organs

In *Juniperus communis*, essential oil is accumulated in the aerial organs of the plant, particularly in the leaves (needles) and cones. These structures serve as the main sites of storage for the aromatic and volatile oil characteristic of the species [75].

2.10.4 Ecological Role of *Juniperus communis* Essential Oil

Essential oils extracted from *Juniperus* species such as *J. communis*, *J. oxycedrus*, *J. pygmaea*, and *J. sibirica* exhibit a wide range of biological activities, including insecticidal, repellent, antifungal, antimicrobial, and antioxidant effects [76]. The main bioactive constituents identified in these oils are monoterpenes and sesquiterpenes, particularly α -pinene, sabinene, β -pinene, limonene, β -myrcene, β -caryophyllene, and germacrene D, which collectively contribute to their ecological defense functions. Among these,

α -pinene and sabinene are frequently associated with strong repellent and insecticidal activity against cereal aphids such as *Rhopalosiphum padi* and *Sitobion avenae*, inducing high mortality rates and significant behavioral avoidance, indicating their role in disrupting herbivore host-plant interactions [76]. Similarly, sesquiterpenes such as β -caryophyllene and cadinene derivatives contribute to antimicrobial and antifungal effects, with inhibition observed against phytopathogens including *Fusarium* spp., *Rhizoctonia solani*, and *Cylindrocarpon pauciseptatum*, suggesting a protective role against soil- and plant-associated microbial infections [76]. In addition, these essential oils demonstrate notable antioxidant activity, particularly in monoterpene-rich chemotypes, which may contribute to the mitigation of oxidative stress under harsh environmental conditions. Overall, the synergistic interaction among multiple terpenoid constituents appears to be responsible for the broad-spectrum bioactivity of *Juniperus* essential oils, supporting their function as chemical defense systems that enhance plant fitness, reduce biotic stress pressure, and improve ecological adaptability in variable environments.

2.11 *Rosmarinus Officinalis*

2.11.1 Taxonomy

The genus *Rosmarinus* belongs to the family Lamiaceae and is placed within the order Lamiales. It is a Mediterranean genus that has traditionally included a small number of species, among which *Rosmarinus officinalis* L. is the most widely distributed and commonly known representative [77,78].

Recent phylogenetic studies have resulted in the merging of *Rosmarinus* with the genus *Salvia*, leading to the currently accepted nomenclature *Salvia rosmarinus* Spenn., while *Rosmarinus officinalis* remains widely used as a synonym in the literature [79].

2.11.2 Geographical Distribution

Rosmarinus officinalis L. is an evergreen aromatic shrub native to the Mediterranean region. It is widely distributed across Mediterranean habitats and is well adapted to diverse climatic and soil conditions, where it can grow and reproduce successfully [77,79].

Within its natural range, rosemary occurs in a variety of environments and displays notable variability in growth form, morphological traits, floral characteristics, and aroma profile, reflecting its ecological adaptability across the Mediterranean basin [79].

2.11.3 Essential Oil-Accumulating Organs

In *Rosmarinus officinalis*, essential oil is primarily accumulated in the leaves, which represent the main plant organ used for oil analysis and extraction. Both mature and young leaves, as well as shoot tips, are commonly used as plant material for essential oil studies, confirming the aerial vegetative tissues as the principal source of volatile compounds [80,81].

Leaves consistently show the highest essential oil content compared to other organs, while stems contribute only negligible amounts and flowers present lower overall yields, although with a distinct chemical profile [81].

2.11.4 Ecological Role of *Rosmarinus officinalis* Essential Oil

Rosmarinus officinalis essential oil is a volatile mixture of bioactive compounds reported to exhibit antifungal, insecticidal, and repellent activities. Experimental evidence showed strong antifungal effects against *Botrytis cinerea*, *Fusarium oxysporum*, and *Alternaria alternata*, including complete inhibition of *B. cinerea*, associated with a composition dominated by 1,8-cineole, α -pinene, and camphor [82]. The

same study also demonstrated significant insecticidal effects against *Callosobruchus maculatus*, with high mortality, reduced fecundity and emergence, and moderate repellency, while molecular docking indicated interactions of borneol and camphor with acetylcholinesterase and α -caryophyllene with β -tubulin [82]. Complementary evidence from a review study confirmed that *R. officinalis* essential oil and its derivatives possess documented bioactivities, including antimicrobial and insect-related effects, and highlighted variability in chemical composition across different studies and extraction conditions [83].

The essential oil of *Rosmarinus officinalis* exerts antipathogenic effects through the synergistic action of its volatile constituents, particularly 1,8-cineole, α -pinene, and β -pinene. According to the reviewed studies, the antimicrobial mechanism is associated with the combined activity of these bioactive compounds, which results in a stronger inhibitory effect compared with the activity of individual components, suggesting a synergistic interaction among essential oil constituents. This mechanism leads to the suppression of microbial proliferation and contributes to the demonstrated antibacterial and antifungal activities against Gram-positive bacteria, Gram-negative bacteria, and fungal species [84].

The taxonomy, geographical distribution, organ-specific accumulation, and ecological roles of the essential oil-producing species discussed above, together with their target organisms, proposed mechanisms, and supporting references, are summarized in Table 1.

Table 1: Ecological role of essential oils.

No.	Species	Ecological Function	Target Organisms/ Stressors	Proposed Mechanism	Reference
1	<i>Thymus vulgaris</i>	Plant defense and pollinator attraction; Insect defense	Pathogens, herbivores, insects, pollinators; <i>Acanthoscelides obtectus</i>	Antimicrobial and insecticidal activity; attraction of bees for cross-pollination; Reduced survival, longevity, oviposition and adult emergence	[13,21]
2	<i>Thymus</i> spp.	Insecticidal activity	<i>Musca domestica</i> and other insects	Toxic effects on insects	[26]
3	<i>Thymus pulegioides</i> /T. serpyllum	Antimicrobial defense	<i>Candida</i> spp.	Synergistic antimicrobial activity	[24]
4	<i>Cinnamomum</i> spp.	Antimicrobial and antifungal defense; Induced resistance	Bacteria, fungi; Microbial pathogens	Membrane disruption, enzyme interference, redox imbalance; Activation of SAR and ISR pathways	[32,33]
5	<i>Piper rivinoides</i>	Chemical defense	Herbivores, pathogens, abiotic stress	Protective monoterpene accumulation in leaves	[36]
6	<i>Piper</i> spp.	Antimicrobial defense	Bacteria; <i>Candida</i> spp.	Antibacterial and antifungal activity	[35]
7	<i>Zingiber zerumbet</i>	Antimicrobial defense	Gram+ and Gram– bacteria	Broad-spectrum antibacterial activity;	[42]
8	<i>Levisticum officinale</i>	Biotic and abiotic stress protection	Pathogens, herbivores, UV radiation	Antioxidant, antimicrobial and structural defense	[47]
9	<i>Spilanthes paniculate</i>	Antifungal and insecticidal defense	<i>Aspergillus</i> , <i>Fusarium</i> , insects	Growth inhibition and neurophysiological disruption	[51–53]
10	<i>Scrophularia oxysepala</i>	Defense against herbivores and oxidative stress	Insects, environmental stressors	Insecticidal activity and antioxidant protection	[57]
11	<i>Salvia officinalis</i>	Antimicrobial defense; Insecticidal and allelopathic activity; Drought adaptation	<i>E. coli</i> , <i>S. aureus</i> , <i>C. albicans</i> ; Insects and competing plants; Water deficit stress	Antibacterial and antifungal activity; Herbivore deterrence and inhibition of seed germination; Increased EO biosynthesis under moderate drought	[63–65]
12	<i>Mentha piperita</i>	Defense and communication	Herbivores, pathogens, pollinators	Deterrent, antimicrobial and signaling functions	[68,70]
13	<i>Juniperus</i> spp.	Insect defense; Antimicrobial defense	<i>R. padi</i> ; <i>S. avenae</i> ; Phytopathogenic fungi	Repellent and insecticidal activity; Antifungal and antimicrobial activity	[76]
14	<i>Rosmarinus officinalis</i>	Antifungal defense; Insecticidal and repellent activity	<i>B. cinerea</i> ; <i>F. oxysporum</i> ; <i>A. alternata</i> ; <i>Callosobruchus maculatus</i>	Growth inhibition of fungi; Interaction with acetylcholinesterase and β -tubulin	[82]

3 Molecular Mechanisms of EO Underlying Anticancer Activity in OSCC

3.1 Essential Oil from *Thymus vulgaris*

3.1.1 Major Bioactive Compounds

The essential oil of *Thymus* species is characterized by a high content of monoterpenes, among which thymol and carvacrol are considered the most important bioactive constituents. The chemical composition of thyme essential oil varies according to species, cultivar, and chemotype, resulting in distinct thymol- and carvacrol-dominant profiles. In *Thymus vulgaris*, cultivars such as ‘Thymia’ and ‘Varico 3’ are classified as thymol-rich chemotypes, whereas ‘Carvalia’ is characterized by a high carvacrol content [21]. Similarly, populations of *Thymus serpyllum* and *Thymus pulegioides* growing in sunny meadow habitats have been reported to exhibit aromatic mono- and bicyclic monoterpenoid chemotypes, with significant concentrations of carvacrol and *p*-cymene [24]. This variability is further supported by intraspecific data: in *T. vulgaris* from Hungary, thymol and *p*-cymene levels shifted between flowering stages [85], while *T. serpyllum* from Azad Kashmir (Pakistan) showed similar phenology-dependent changes in thymol/carvacrol ratios [86]. At the habitat level, *T. serpyllum* from ecologically distinct Kazakhstani sites ranged from carvacrol-dominant to geraniol-dominant chemotypes, highlighting the influence of microhabitat conditions on essential oil chemistry [87].

3.1.2 Antitumoral Activity in OSCC

Thymus vulgaris essential oil has been shown to exert a concentration-dependent effect on human OSCC cells. At higher concentrations, it inhibits the proliferation of UMSCC1 tumor cells, whereas at subtoxic doses it may paradoxically stimulate cellular growth. Mechanistically, the cytotoxic effects have been associated with modulation of pathways involved in interferon signaling, N-glycan biosynthesis, and ERK5 signaling, suggesting a multifactorial molecular basis for its antitumoral activity [12].

Thymol has demonstrated cytotoxic activity against OSCC cell lines, including Cal27, SCC4, and SCC9, with IC₅₀ values ranging from 300–550 μ M. Its antitumor effects are characterized by mitochondrial transmembrane potential ($\Delta\Psi$ m) depolarization, induction of apoptosis, and a reduction in subcutaneous tumor volume.

In vitro and *in vivo* studies have shown that thymol exerts significant and sustained antiproliferative effects, including marked inhibition of Cal27-derived tumor growth in xenograft models. Similar antitumor activity observed in HeLa-derived xenografts suggests that its effects are not restricted to OSCC. Mechanistically, thymol was initially associated with TRPA1-mediated calcium influx in Cal27 cells; however, this response was absent in HeLa cells, and pharmacological blockade of TRPA1 did not alter cytotoxicity. Instead, mitochondrial dysfunction and $\Delta\Psi$ m depolarization were identified as the primary drivers of thymol-induced apoptosis, indicating a TRPA1-independent, mitochondria-mediated mechanism of cell death and supporting its potential broad-spectrum anticancer activity [10].

Carvacrol, a natural isopropyl cresol found in Lamiaceae essential oils (e.g., *Origanum* and *Thymus*), has shown significant antitumor activity in OSCC. In SCC-25 cells, carvacrol inhibited proliferation in a concentration-dependent manner, as assessed by MTT assay [9]. *In vivo*, carvacrol reduced DMBA-induced oral carcinogenesis in rats, with decreased expression of PCNA and Bcl-2, supporting its antiproliferative and pro-apoptotic effects and its potential as a natural therapeutic agent for OSCC [88].

3.2 Essential Oil from *Cinnamomum* spp.

3.2.1 Major Bioactive Constituents

The essential oils of *Cinnamomum* species exhibit considerable chemical diversity, with distinct chemotypes characterized by different dominant constituents. In *Cinnamomum camphora*, the major chemotypes are defined by eucalyptol, camphor, linalool, nerolidol, and selina, while methyl isoeugenol, methyl eugenol, selinene, and borneol occur as less common chemotypes. Some *C. camphora* populations have been reported to accumulate exceptionally high levels of methyl isoeugenol, exceeding 80% of the total essential oil composition [89].

In *Cinnamomum verum*, the essential oil is predominantly composed of benzenoids and phenylpropanoids. The major constituents include eugenol, benzyl benzoate, (E)-cinnamyl acetate, and (E)-cinnamaldehyde, with eugenol and cinnamaldehyde recognized as the principal bioactive compounds responsible for many of the biological and aromatic properties of cinnamon essential oil. The relative abundance of these constituents may vary considerably among cultivated and commercial samples, reflecting the existence of different chemotypes within the species [29].

3.2.2 Antitumoral Activity in OSCC

Cinnamon essential oil and its main component cinnamaldehyde have demonstrated cytotoxic activity against OSCC, with IC₅₀ values of 90.40 µg/mL (24 h) and 42.95 µg/mL (48 h). The oil significantly inhibits proliferation, migration, and invasion of oral cancer cells, consistent with previous reports of antitumor effects in OSCC cell lines such as SCC12.

Morphological and histological analyses show features of apoptosis, including cellular shrinkage, chromatin condensation, membrane blebbing, and formation of apoptotic bodies, alongside a reduction in nuclear area factor in treated groups compared to controls. These findings confirm both early and late apoptotic processes induced by cinnamon oil [14].

Additionally, cinnamon essential oil has been reported to exert anticancer effects in head and neck squamous cell carcinoma by attenuating epidermal growth factor receptor (EGFR) tyrosine kinase signaling, supporting its broader antitumor potential [90].

Eugenol, the major active constituent of clove essential oil, exhibits dose-dependent cytotoxic effects against OSCC, particularly SCC-4 and SCC-9 cells, as well as gingival fibroblasts. It induces a significant reduction in cell viability, with SCC-4 cells being more sensitive than normal gingival fibroblasts, and produces clear morphological changes consistent with apoptosis, including cell rounding, loss of confluency, and chromatin condensation. These effects are accompanied by increased expression of pro-apoptotic genes such as Bax and Bad, indicating activation of apoptosis in tongue squamous carcinoma cells [91].

In SCC9 cells, eugenol significantly reduces proliferation, migration, and invasion, partly through downregulation of MMP-2 and MMP-9 and modulation of apoptotic regulators such as Bcl-2, Bax, cleaved caspase-3, and PARP. It also targets macrophage migration inhibitory factor (MIF), and its overexpression reverses the antitumor effects of eugenol, indicating a key mechanistic role in OSCC suppression [92].

Additionally, in SCC-9 cell line, eugenol inhibits tumor proliferation and colony formation while inducing G0/G1 cell cycle arrest via modulation of the p21/p27/cyclin D1 axis in a p53-independent manner. It also suppresses cell migration through MMP1/3 downregulation and is associated with inhibition of P38/STAT5/NF-κB signaling pathways, supporting its broader anticancer potential in OSCC [93].

3.3 Essential Oil from *Piper rivinoides*

3.3.1 Major Bioactive Constituents

The essential oil of *Piper rivinoides* is predominantly composed of monoterpenes, with α -pinene and β -pinene identified as the major bioactive constituents. These compounds represent the highest proportion of the essential oil throughout the year, despite seasonal variations in their relative abundance. The content of α -pinene ranges from 34.78% to 53.87%, while β -pinene varies between 15.24% and 47.71%, highlighting their dominant contribution to the chemical profile of the species and their potential role in its biological activities [94].

3.3.2 Antitumoral Activity in OSCC

Crude EOs from *Piper rivinoides*, as well as their major constituents and an enriched fraction (EF), have demonstrated cytotoxic activity against OSCC. The oils are mainly composed of (-)- α -pinene, (-)- β -pinene, and limonene. Overall, the crude EOs exhibited IC₅₀ values lower than those of most isolated compounds, although (-)- β -pinene showed strong cytotoxicity comparable to the whole extract in OSCC cells. The enriched fraction displayed improved selectivity compared to crude EOs and even carboplatin, suggesting potential for anticancer development in OSCC.

Mechanistically, (-)- β -pinene induces apoptotic cell death characterized by morphological alterations such as membrane blebbing, nuclear pyknosis, and cell shrinkage. Apoptosis was further confirmed by caspase involvement, as inhibition with pancaspase (Z-VAD) and caspase-3 inhibitor (Z-DEVD) significantly reduced cell death, indicating a caspase-dependent apoptotic pathway in oral tongue cancer cells [15].

3.4 Essential Oil from *Zingiber zerumbet*

3.4.1 Major Bioactive Constituents

The essential oil of *Zingiber zerumbet* is characterized by a complex terpenoid composition that varies according to the plant organ. Rhizome essential oil is predominantly composed of sesquiterpenoids, with zerumbone being the major bioactive constituent, accompanied by humulene, humulene oxides, β -caryophyllene, and α -caryophyllene. In contrast, essential oils obtained from the aerial parts (leaves, stems, and inflorescences) are rich in nerolidol, trans-phytol, β -caryophyllene, linalool, and pinenes, while containing lower amounts of zerumbone. These compounds are considered key contributors to the biological activities associated with *Z. zerumbet* essential oil [38].

3.4.2 Antitumoral Activity in OSCC

The essential oil of *Zingiber zerumbet*, characterized by 18 identified components with zerumbone (48.39%), humulene (17.05%), and camphene (5.83%) as major constituents, has demonstrated strong antiproliferative activity against OSCC. It inhibited the growth of H103 and ORL-204 OSCC cell lines with IC₅₀ values of 1.93 and 1.13 μ g/mL, respectively, indicating high cytotoxic potency.

Mechanistic studies in ORL-204 cells confirmed that treatment with the essential oil induces apoptosis and alters cell cycle distribution. Further evidence suggests activation of both intrinsic and extrinsic apoptotic pathways, together with cell cycle arrest at the S and G2/M phases, supporting a multi-targeted antitumor mechanism. Overall, these findings indicate that *Z. zerumbet* essential oil, particularly its major compound zerumbone, represents a promising candidate for further development as an anticancer agent in OSCC [17].

3.5 Essential Oil from *Levisticum officinale*

3.5.1 Major Bioactive Constituents

Root essential oil of *Levisticum officinale* is predominantly composed of monoterpenes and phthalides, which represent its main classes of volatile constituents. Phthalides are considered characteristic chemotaxonomic markers of the species and, together with monoterpenes, contribute substantially to its biological activity [95]. Among the phthalide fraction, (Z)-ligustilide and neocnidilide are the most representative constituents in aerial parts, playing a major role in defining the chemical profile of the species. The composition of these constituents shows marked organ-dependent variability. In aerial parts, the dominant compounds include pentyl cyclohexa-1,3-diene (22.7–28.1%), (Z)-ligustilide (24.5–26.0%), and neocnidilide (15.9–23.0%), whereas root essential oil is mainly characterized by p-menth-1-en-8-ol acetate (21.1–42.1%) and Z- β -ocimene (13–28.1%), with lower levels of ligustilide derivatives—(Z)-ligustilide (0.8–5.8%) and neocnidilide (4.8–11.6%). This clear shift in composition between plant organs highlights a pronounced chemotypic variation within the species, which may influence its biological properties [96].

3.5.2 Antitumoral Activity in OSCC

Levisticum officinale (lovage) essential oil has been shown to inhibit the growth of human head and neck squamous cell carcinoma (HNSCC), including UMSCC1 cells, with an IC₅₀ value of 292.6 μ g/mL.

Mechanistically, its antiproliferative effects are associated with modulation of key signaling pathways involved in tumor progression, including extracellular signal-regulated kinase 5 (ERK5) signaling, integrin-linked kinase (ILK) signaling, p53 signaling, and virus entry via endocytic pathways. Gene expression profiling further indicated that apoptosis-, cell cycle-, and cancer-related genes were among the most affected, supporting a broad regulatory impact on cellular growth and survival processes. Overall, *L. officinale* essential oil demonstrates antiproliferative activity against HNSCC cells through multi-pathway modulation [18].

3.6 Essential Oil from *Spilanthes paniculata*

3.6.1 Major Bioactive Constituents

The essential oil of *Spilanthes paniculata* is predominantly composed of sesquiterpenes and oxygenated sesquiterpenes. Subhashree et al. [51] reported that GC–MS analysis identified spathulenol, germacrene D, (E)-caryophyllene, δ -amorphene, β -bisabolene, and limonene among the principal volatile constituents. Among these, spathulenol was the most abundant compound (6.90–19.08%), followed by germacrene D (3.49–10.77%), (E)-caryophyllene (1.53–10.98%), and δ -amorphene (0.33–15.32%). Furthermore, Satapathy et al. [19] highlighted spathulenol, δ -amorphene, β -bisabolene, limonene, and (E)-nerolidol as key bioactive constituents potentially responsible for the anticancer activity of *S. paniculata* essential oil.

3.6.2 Antitumoral Activity in OSCC

The flower essential oil of *Spilanthes paniculata* has demonstrated significant cytotoxic activity against oral cancer cells, reducing cell viability in a dose-dependent manner with an IC₅₀ value of 113.95 μ g/mL. Apoptosis assays indicated that the flower oil was approximately 2.5-fold more effective in inducing early apoptosis at 50 μ g/mL compared to the leaf essential oil, highlighting tissue-specific variability in anticancer potency.

The anticancer potential was further confirmed by orosphere formation assays, which showed strong inhibition of tumor sphere growth. Molecular docking analysis suggested that spathulenol, one of the major

constituents, may interact with the p53 protein via strong hydrogen bonding ($<2.5 \text{ \AA}$), indicating a possible mechanism involving p53-related apoptotic regulation. Overall, the flower essential oil exhibited superior antiproliferative and pro-apoptotic effects compared to leaf extracts in oral cancer models [19].

3.7 Essential Oil from *Scrophularia oxysepala*

3.7.1 Major Bioactive Constituents

The essential oil of *Scrophularia oxysepala* analyzed by GC–MS is characterized by a mixed profile dominated by oxygenated terpenoids and aromatic/phenylpropanoid derivatives. The major constituents include phytol (~25.3%), methyl benzyl alcohol (~9.3%), dehydrodieugenol (~6.7%), methyl benzaldehyde (~5.3%), and eugenol (~1.3%), alongside minor aliphatic alcohols and hydrocarbons, indicating a chemical profile not typically rich in monoterpenes but rather in oxygenated and phenolic-derived volatiles [97]. Similarly, essential oils from other *Scrophularia* species are reported to be enriched in sesquiterpenes and oxygenated volatile compounds such as β -elemene, spathulenol, and farnesyl acetone, supporting a genus-level tendency toward sesquiterpenoid-dominated EO profiles [98].

3.7.2 Antitumoral Activity in OSCC

Scrophularia oxysepala essential oil has shown significant time- and concentration-dependent cytotoxic effects against the OECM-1 oral cancer cell line. Treated cells exhibited marked morphological changes consistent with apoptosis and cell death, indicating strong antitumor activity.

Mechanistically, the essential oil increased apoptosis rates through modulation of key apoptosis-related genes, including upregulation of BAX and SMAC and downregulation of BCL2 and SURVIVIN, suggesting activation of intrinsic apoptotic pathways. Overall, *S. oxysepala* essential oil demonstrates notable cytotoxic and pro-apoptotic effects in oral cancer cells, supporting its potential anticancer relevance in OSCC models [20].

3.8 Essential Oil from *Salvia officinalis*

3.8.1 Major Bioactive Constituents

Salvia officinalis essential oil is rich in bioactive constituents such as α -thujone, β -thujone, camphor, and 1,8-cineole, along with phenolic compounds including rosmarinic acid, carnosic acid, and carnosol, which collectively contribute to its pharmacological profile [59]. The α -thujone typically ranges from approximately 18.8% to 42.9%, camphor from 10.7% to 27.1%, and 1,8-cineole from 4.7% to 15.6%, depending on geographic origin, cultivation conditions, and phenological stage [63–65].

3.8.2 Antitumoral Activity in OSCC

Salvia officinalis essential oil, rich in monoterpenes such as thujone, β -pinene, and 1,8-cineole, has been reported to possess multiple biological activities, including antioxidant, anti-inflammatory, and cytotoxic effects against cancer cell lines, supporting its potential anticancer relevance [59].

In human HNSCC, including UMSCC1 cells, sage essential oil has demonstrated dose-dependent cytotoxicity. At low concentrations, it increased cell viability, whereas concentrations above the IC_{50} value of 135 $\mu\text{g/mL}$ resulted in a marked reduction in cell survival, indicating a biphasic, concentration-dependent effect [99].

Mechanistically, *S. officinalis* essential oil modulates several tumor-related signaling pathways, including aryl hydrocarbon receptor signaling, G1/S cell cycle checkpoint regulation, and p53 signaling, with

additional effects on genes involved in cell proliferation, apoptosis, DNA repair, and cell cycle control [99]. Overall, these findings suggest that sage essential oil exerts antiproliferative effects through multi-pathway regulation, supporting its anticancer potential in OSCC.

3.9 Essential Oil from *Mentha piperita*

3.9.1 Major Bioactive Constituents

The essential oil of *Mentha × piperita* is predominantly composed of p-menthane-type monoterpenes, which define its characteristic chemical profile and commercial value [69]. The most abundant constituents include menthol, menthone, limonene, linalool, and pulegone, alongside other major volatile compounds such as 1,8-cineole, α -pinene, β -pinene, myrcene, sabinene, γ -terpinene, and β -caryophyllene [68,100]. These phytochemicals largely determine the plant's biological activity and contribute to its well-documented pharmacological properties.

3.9.2 Antitumoral Activity in OSCC

Mentha piperita essential oil has demonstrated significant cytotoxic activity *in vitro* against OSCC-related cancer models. In experimental studies, peppermint oil induced a strong, dose-dependent reduction in tumor cell viability, accompanied by morphological changes consistent with cytotoxic stress and apoptosis, including cell shrinkage, membrane damage, and loss of adhesion. The effect was reported to be concentration-dependent, with near-complete loss of viability at higher doses. These findings support the potential antitumoral activity of *M. piperita* essential oil in head and neck cancer models, including OSCC-related cellular systems [13,101].

3.10 Essential Oil from *Juniperus communis*

3.10.1 Major Bioactive Constituents

The EOs of *Juniperus species* (cultivated *Juniperus communis* clones and wild *J. communis*, *J. recurva*, *J. indica*) are mainly composed of monoterpene hydrocarbons (49.1–82.8%), which represent the dominant chemical class [72]. The principal bioactive constituents consistently reported include α -pinene, β -pinene, sabinene, limonene, and myrcene, along with dl-limonene and bornyl acetate, all contributing to their biological and aromatic properties [102].

Sabinene, α -pinene, and limonene are the most abundant compounds overall, with sabinene dominating especially in wild species (*J. recurva*, *J. indica*) (55–59%) and also being high in cultivated clones of *J. communis* (37–47%). A distinct chemotype was observed in clone-7, characterized by elevated α -pinene (41.3%) and limonene (32.8%) [72]. Overall, *Juniperus* EOs show strong chemical variability influenced by species, genotype, and environmental factors [72,102].

3.10.2 Antitumoral Activity in OSCC

The essential oil of *Juniperus communis* has been investigated for its anticancer potential in OSCC models. Lazarević et al. [13] reported that essential oil mixtures including *J. communis* significantly reduced the viability of SCC-25 oral carcinoma cells in a dose-dependent manner using MTT assays, indicating cytotoxic activity against OSCC cells [13]. Direct mechanistic evidence in oral cancer has been reported for a related species: *Juniperus indica* extract reduced viability in OECM-1, SAS and SCC-25 oral cancer cells, and in OECM-1 cells specifically induced cell cycle arrest, activated the caspase cascade, and showed a synergistic cytotoxic effect when combined with cisplatin, partly via suppression of Akt/mTOR signaling [103].

3.11 Essential Oil from *Rosmarinus officinalis*

3.11.1 Major Bioactive Constituents

The essential oil of *Rosmarinus officinalis* L. contains a complex mixture of volatile compounds, with the major constituents identified as 1,8-cineole, α -pinene, camphor, camphene, and β -pinene [104]. These compounds are largely responsible for its biological activities, including notable antibacterial and cytotoxic effects, particularly against human cancer cell lines. In addition, the essential oil exhibits strong antioxidant potential, highlighting its ability to neutralize free radicals and its relevance as a rich natural source of bioactive antioxidants [104,105].

3.11.2 Antitumoral Activity in OSCC

The essential oil of *Rosmarinus officinalis* has demonstrated *in vitro* cytotoxic activity against OSCC models. In a comparative study evaluating multiple aromatic plant essential oils, Lazarević et al. [13] reported that *R. officinalis* essential oil significantly reduced cell viability in both SCC-25 OSCC cell lines and primary OSCC cultures using MTT and Neutral Red assays, indicating a clear dose-dependent cytotoxic effect [13]. Among the tested oils, rosemary essential oil was identified as one of the most active in inhibiting OSCC cell proliferation, confirming its consistent *in vitro* cytotoxic activity against OSCC.

The chemical diversity summarized in Table 2 and visualized in the heatmap (Fig. 1) highlights both the compound-level variability and the chemotype divergence among the essential oil-producing species discussed in this review. Each taxon is characterized by a distinct dominant constituent or class of constituents: thymol and p-cymene in *Thymus vulgaris*, carvacrol and thymol in *Thymus serpyllum*, 1,8-cineole and α -pinene in *Rosmarinus officinalis*, α -thujone and camphor in *Salvia officinalis*, α -pinene and β -pinene in *Piper rivinoides*, sabinene and α -pinene in *Juniperus communis*, zerumbone in *Zingiber zerumbet*, cinnamaldehyde and eugenol in *Cinnamomum verum*, camphor and linalool in *Cinnamomum camphora*, α -terpinyl acetate and (Z)-ligustilide in *Levisticum officinale*, and spathulenol and germacrene D in *Spilanthes paniculata*. Visual inspection of the dominant constituents displayed in the heatmap (Fig. 1) indicates the closest chemical relationship was observed between *Thymus vulgaris* and *Thymus serpyllum*, consistent with their shared thymol/carvacrol/p-cymene monoterpene chemistry, while a notable convergence was also evident between the phylogenetically unrelated *Piper rivinoides* and *Rosmarinus officinalis*, both dominated by α - and β -pinene. In contrast, the most divergent chemical profiles were found between *Juniperus communis* and *Spilanthes paniculata*, reflecting the contrast between a monoterpene hydrocarbon-dominated profile and a sesquiterpene/oxygenated sesquiterpene-dominated profile, respectively. This pattern illustrates that chemical similarity across the reviewed species is driven more by shared biosynthetic pathways and dominant terpenoid classes than by taxonomic relatedness. Collectively, this extensive chemical variability and chemotype divergence, compounded by differences in plant organ, developmental stage, and geographic origin, underscore the difficulty of achieving standardized essential oil compositions and, consequently, of ensuring reproducibility across independently conducted studies.

Table 2: Chemical composition (major volatile constituents), essential oil yield, and extraction method reported for the plant species and populations discussed in this review.

<i>Thymus vulgaris</i>	Thymol	p-cymene	Carvacrol	γ-Terpinene	Linalool							EO Yield	Extraction Method	Ref.
commercial oil from Sigma-Aldrich cultivar 'Standard Winter'; herb (upper dried parts); organic cultivation, experimental field, Warsaw, Poland; 2-year-old plants, harvested at early flowering, June 2018	43.52%	31.65%	5.11%		5.38%							NR	NR	[25]
beginning of flowering (collected 23 May 2019), Szigetvár, Hungary	55.81%	12.89%	2.3%	15.18%	1.46%							8450 µL, from fresh plant	Hydrodistillation (100 g dried plant material + 1000 mL distilled water, 3 h)	[85]
end of flowering (collected 12 June 2019), Szigetvár, Hungary	54.21%	20.64%	2.9%	6.01%	2.15%							3920 µL, from fresh plant	Hydrodistillation (100 g dried plant material + 1000 mL distilled water, 3 h)	[85]
blossoms/leaves/stipes	33.0%	23.8%		15.4%	2.6%							NR	Steam distillation (100° C)	[12]
<i>Thymus serpyllum</i>	Carvacrol	Thymol	Geraniol	α-terpineol	Borneol	Linalool	1,8-cineole	p-cymene	Ledol	Thymoquinone	Spathulenol	EO Yield	Extraction method	Ref.
Pir Chanassi, District Muzaffarabad, Azad Kashmir, ~12,000 ft; before flowering, collected June–July 2007	11.2%	18.8%			1.6%		14.0%	1.1%	0.2%	not detected before flowering	1.3%	NR	Hydrodistillation (3 replicates, 4 h, normal pressure, Clevenger-type apparatus)	[86]
Pir Chanassi, District Muzaffarabad, Azad Kashmir (Pakistan-administered), ~12,000 ft; at flowering, collected June–July 2007	12.4%	16.5%			3.8%		18.0%	1.3%	7.3%	2.6%	2.1%	NR	Hydrodistillation (3 replicates, 4 h, normal pressure, Clevenger-type apparatus)	[86]
aerial part, full-flowering stage, Birch forest edge	55.19%	13.21%			1.15% (endo-Borneol)			11.24%				1.30%	Hydrodistillation (Clevenger, 3 h, 100 g dried material)	[87]
aerial part, full-flowering stage, Clearing, mixed grasses	38.42%	28.56%			0.92% (endo-Borneol)			12.69%				1.30%	Hydrodistillation (Clevenger, 3 h, 100 g dried material)	[87]
aerial part, full-flowering stage, Forest-encircled clearing	55.85%	11.31%						13.33%				1.20%	Hydrodistillation (Clevenger, 3 h, 100 g dried material)	[87]
aerial part, full-flowering stage, Dry clearing/slope, Kamenucha mountain	1.22%	5.11%	55.93% (trans-geraniol)					1.28%				1.25%	Hydrodistillation (Clevenger, 3 h, 100 g dried material)	[87]
aerial part, full-flowering stage, Clearing, fresh/moist conditions	25.68%	31.74%			3.02%			13.34%				0.70%	Hydrodistillation (Clevenger, 3 h, 100 g dried material)	[87]
aerial part, full-flowering stage, Slope, valley micro-site	6.21%	58.25%			2.43%			13.44%				0.97%	Hydrodistillation (Clevenger, 3 h, 100 g dried material)	[87]
aerial part, full-flowering stage, Slope and dry meadow	6.08%	44.30%			2.70%		1.87%	25.46%				0.40%	Hydrodistillation (Clevenger, 3 h, 100 g dried material)	[87]
aerial part, full-flowering stage, Slope, variable conditions	35.31%	24.18%			1.57%		1.57%	14.75%				1.40%	Hydrodistillation (Clevenger, 3 h, 100 g dried material)	[87]
Bila skelja	6%		5%	2.5%		63%						0.9% (9 mL/kg)	Hydrodistillation (Clevenger, 2 h)	[24]
Strach village	~20%		~15%	~20%	~9.5%			~10%				0.7% (7 mL/kg)	Hydrodistillation (Clevenger, 2 h)	[24]
near Trostyanets village	6%		35%	17%	7.5%							0.8% (8 mL/kg)	Hydrodistillation (Clevenger, 2 h)	[24]
<i>Thymus pulegioides</i>	Geraniol	Carvacrol	α-terpineol	α-terpinene	Borneol	p-cymene						EO Yield	Extraction method	Ref.
Pustomyty	22%	17%	13%	8%	7%	6%						0.8%	Hydrodistillation (Clevenger, 2 h)	[24]

Table 2: *Cont.*

<i>Cinnamomum cassia</i>	Cinnamal- dehyde	Eugenol	Cinnamyl acetate	Linalool	β - Caryophyllene	Benzyl benzoate	Clovene	Eugenol acetate	Coumarin			EO Yield	Extraction method	Ref.
	60–90%	5–15%	5–10%	1–5%	1–3%	0.5–2%	0.5–2%	0.3–1%	0.05–0.5%			NR	NR	[33]
Bark	86.92%											NR	Hydrodistillation (Clevenger-type, 50 g bark, 100° C, 6 h)	[90]
<i>Cinnamomum verum</i>	Cinnamal- dehyde	Eugenol	Linalool	Benzyl benzoate	Cinnamyl acetate	Eucalyptol (1,8- cineole)	β - Caryophyllene	trans- Cinnamyl acetate	Caryophyllene	α -Terpineol	α -Pinene	EO Yield	Extraction method	Ref.
bark, Sri Lanka	41.3%	4.0%	18.3%	1.2%		6.8%		3.3%	3.3%	3.2%	2.0%	NR	Steam distillation	[32]
leaves, cultivated, dried, Curuçá (PA), Brazil	60–90%	38.42%	2–6%	0.5–2%	3–8%		1–4%					NR	NR	[33]
leaves, cultivated, dried, Benevides (PA), Brazil	2.4%	2.13%	3.66%	76.51%				4.43%			1.18%	1.67%	Hydrodistillation (Clevenger-type, 3 h)	[29]
leaves, cultivated, dried, Belém (PA), Brazil	1%	91%	0.54%	0.29%				0.33%			0.23%	1.90%	Hydrodistillation (Clevenger-type, 3 h)	[29]
leaves, cultivated, dried, Maranhãozinho (MA), Brazil	3.51%	0.7%		44.11%				14.94%			1.52%	1.30%	Hydrodistillation (Clevenger-type, 3 h)	[29]
	19.74%	1.07%	1.97%	15.83%				32.1%			2.89%	0.54%	Hydrodistillation (Clevenger-type, 3 h)	[29]
<i>Cinnamomum zeylanicum</i>	Cinnamal- dehyde	Eugenol	Cinnamyl acetate	Linalool	β - Caryophyllene	Benzyl benzoate	Clovene	Eugenol acetate	Coumarin			EO Yield	Extraction method	Ref.
	60–90%	5–15%	5–10%	1–5%	1–3%	0.5–2%	0.5–2%	0.3–1%	0.05–0.5%			NR	NR	[33]
<i>Cinnamomum burmannii</i>	Cinnamal- dehyde	Eugenol	Cinnamyl acetate	Linalool	β - Caryophyllene	Benzyl benzoate	Clovene	Eugenol acetate	Coumarin			EO Yield	Extraction method	Ref.
	55–85%	10–20%	5–12%	2–7%	1–5%	0.5–2%	0.5–2%	0.3–1%	0.05–0.5%			NR	NR	[33]
<i>Cinnamomum camphora</i>	Eucalyptol	Linalool	Camphor	Borneol	trans- Nerolidol	Selina-6- en-4-ol	Methyl isoeugenol	α -Terpineol	α -Pinene			EO Yield	Extraction method	Ref.
leaves, fresh, Shixing, Guangdong, China	65.33%	1.59%		0.13%				9.25%	2.91%			NR	Hydrodistillation (modified Clevenger-type, 3 h, ~100 g fresh leaves)	[89]
leaves, fresh, Youxi, Fujian, China	0.03%	93.73%	0.23%		0.02%	0.02%	0.43%	0.27%				NR	Hydrodistillation (modified Clevenger-type, 3 h, ~100 g fresh leaves)	[89]
leaves, fresh, Changsha, Hunan, China	1.63%		84.35%	0.22%	0.23%			1.03%	0.63%			NR	Hydrodistillation (modified Clevenger-type, 3 h, ~100 g fresh leaves)	[89]
leaves, fresh, Anfu, Jiangxi, China	0.38%	0.39%	0.75%	0.09%	60.30%	0.11%	0.32%	0.23%	0.06%			NR	Hydrodistillation (modified Clevenger-type, 3 h, ~100 g fresh leaves)	[89]
leaves, fresh, Quanzhou, Guangxi, China	1.77%	2.87%	23.37%	52.22%				1.32%	1.56%			NR	Hydrodistillation (modified Clevenger-type, 3 h, ~100 g fresh leaves)	[89]
leaves, fresh, Gaofeng, Guangxi, China	0.07%	0.44%	0.01%		0.04%	0.01%	71.99%	0.43%				NR	Hydrodistillation (modified Clevenger-type, 3 h, ~100 g fresh leaves)	[89]
leaves, fresh, Gaofeng, Guangxi, China		0.02%	0.02%	0.15%	0.43%	71.20%	0.30%	0.15%				NR	Hydrodistillation (modified Clevenger-type, 3 h, ~100 g fresh leaves)	[89]

Table 2: *Cont.*

<i>Piper rivinoides</i>	α -Pinene	β -Pinene	β -Caryophyllene									EO Yield	Extraction method	Ref.
leaves, vegetative stage, Pedra Branca State Park, Rio de Janeiro, Brazil	31.90%	20.96%										0.82% (w/w)	Hydrodistillation (Clevenger, 2 h, 100 g plant material)	[37]
leaves, wild, Serra da Tiririca-Niterói, Rio de Janeiro state; collected January 2019 (summer)	34.78%	44.30%	1.70%									0.16% (w/w)	Hydrodistillation (Clevenger, 100 g fresh leaves, 2 h)	[94]
leaves, wild, Serra da Tiririca-Niterói, Rio de Janeiro state; collected October 2019 (spring)	51.64%	15.24%	1.02%									1.36% (w/w)	Hydrodistillation (Clevenger, 100 g fresh leaves, 2 h)	[94]
leaves, wild, Serra da Tiririca-Niterói, Rio de Janeiro state; collected August 2019 (winter)	53.87%	18.07%	0.49%									0.77% (w/w)	Hydrodistillation (Clevenger, 100 g fresh leaves, 2 h)	[94]
leaves, wild, Rainforest of Tijuca, Rio de Janeiro state; collected August 2019 (winter)	38.06%	47.71%	0.81%									0.72% (w/w)	Hydrodistillation (Clevenger, 100 g fresh leaves, 2 h)	[94]
<i>Zingiber zerumbet</i>	Zerumbone	humulene	camphene									EO Yield	Extraction method	Ref.
rhizomes, Manaus/AM, Brazil	87.93%											5% (oil mass/raw material mass ratio)	Hydrodistillation (Clevenger, 2 L, material:water ratio 1:4, 6 h from boiling point)	[42]
fresh/mature rhizomes	48.39%	17.05%	5.83%									NR	Hydrodistillation	[17]
<i>Levisticum officinale</i>	α -Terpinyl acetate	β -Phellandrene	(Z)- β -Ocimene	β -Myrcene	Neocnidilide	(Z)-Ligustilide	β -Pinene	α -Terpineol	pentyl cyclohexa-1,3-diene	p-menth-1-en-8-ol acetate	p-Cymene	EO Yield	Extraction method	Ref.
leaves, commercial oil—Brazil; plant imported from Hungary	36.67%	36.21%	3.22%	10.66%				4.61%				NR	Steam distillation	[46]
aerial parts, Mount Hezar, Kerman province, Iran	52.85%	10.26%	3.99%		10.12%	6.22%	5.10%				0.75%	2.8% v/w	Hydrodistillation (Clevenger, 3 h, on aerial parts, 150 g)	[48]
Leaves	48.15%	13.16%		5.07%		3.86%	0.41%					NR	Steam distillation (100° C)	[18]
aerial parts, flowering and fruiting stages					15.9–23.0%	24.5–26.0%			22.7–28.1%			2.5–3.0% v/w (range reported across organs/stages)	Hydrodistillation	[96]
root, flowering and fruiting stages			13–28.1%		4.8–11.6%	0.8–5.8%			2.2–2.4%	21.1–42.1%		2.5–3.0% v/w (range reported across organs/stages)	Hydrodistillation	[96]
<i>Spilanthes paniculate</i>	Spathulenol	Germaacrene D	β -Bisabolene	2-Tridecanone	(E)-Caryophyllene	Limonene	(E)-iso- γ -Bisabolene	Farnesol <(2Z, 6Z)>	δ -Amorphene	β -Atlantol	E- γ -Cadinene	EO Yield	Extraction method	Ref.
leaves, Khordha, Bhubaneswar, Odisha, India	12.86%	10.77%	9.90%	3.68%	10.98%		18.90%		0.33%	3.60%		0.18% (v/w)	Hydrodistillation (Clevenger, 500 mL distilled water, 6 h; triplicate)	[51]
flowers, Khordha, Bhubaneswar, Odisha, India	19.08%	10.23%	2.70%	13.48%	8.44%	10.89%			15.32%	0.14%		0.25% (v/w)—maximum yield among organs	Hydrodistillation (Clevenger, 500 mL distilled water, 6 h; triplicate)	[51]
stems, Khordha, Bhubaneswar, Odisha, India	17.94%	3.49%	5.11%		1.53%			17.60%		11.90%		0.10% (v/w)	Hydrodistillation (Clevenger, 500 mL distilled water, 6 h; triplicate)	[51]
roots, Khordha, Bhubaneswar, Odisha, India	6.90%	4.62%	4.99%		1.75%				0.44%			0.03% (v/w)—minimum yield among organs	Hydrodistillation (Clevenger, 500 mL distilled water, 6 h; triplicate)	[51]
whole plant, Gaoligong Mountains, Yunnan, China	1.93%	3.12%	7.15%	2.26%		2.82%					10.64%	0.58% v/w (2.9 mL from 500 g dried powder)	Hydrodistillation (Clevenger, 3 h)	[54]

Table 2: *Cont.*

<i>Scrophularia oxysepala</i>	Phytol	6,10,14-trimethyl-2-pentadecanone	Methyl benzyl alcohol	2,4-Dimethyl eicosane	Dehydrodieugenol	Hexacosane	Pentadecane	Eicosane	Methyl benzaldehyde	Palmitaldehyde, diallyl acetone	Eugenol	EO Yield	Extraction method	Ref.
dry aerial parts, Gareh Dag mountain, Kalibar, East Azerbaijan province, Iran	25.3%	11.4%	9.3%	8.6%	6.7%	6.6%	6.3%	6.3%	5.3%	3.3%	1.3%	0.1% v/w	Hydrodistillation (Clevenger-type apparatus, 4 h)	[97]
<i>Salvia officinalis</i>	α -Thujone	Camphor	1,8-Cineole	β -Thujone	Camphene	α -Humulene	Viridiflorol	α -Pinene	Borneol	α -Terpinyl acetate	β -Pinene	EO Yield	Extraction method	Ref.
aerial parts, grown in the Upper Meso-Mediterranean bioclimatic zone, Murcia, Spain	22.8%	19.8%	10.6%	6.1%	5.6%	6.2%						0.8–1.5% (v/w, general value for all 4 oils)	Hydrodistillation (Clevenger, 3 h)	[63]
aerial parts, grown in the Lower Meso-Mediterranean bioclimatic zone, Murcia, Spain	41.7%	16.0%	4.7%	7.8%	6.0%					6.5%		0.8–1.5% (v/w, general value for all 4 oils)	Hydrodistillation (Clevenger, 3 h)	[63]
aerial parts, grown in the Upper Meso-Mediterranean bioclimatic zone, Murcia, Spain	25.5%	10.7%	15.6%	14.8%							5.3%	0.8–1.5% (v/w, general value for all 4 oils)	Hydrodistillation (Clevenger, 3 h)	[63]
aerial parts, grown in the Lower Meso-Mediterranean bioclimatic zone, Murcia, Spain	42.9%	14.2%	7.1%	7.5%	4.9%			5.1%				0.8–1.5% (v/w, general value for all 4 oils)	Hydrodistillation (Clevenger, 3 h)	[63]
leaves; Chott Mariem, Central-East Tunisia	18.83%	25.14%	14.14%	4.46%		2.48%	7.98%		2.81%			0.66% (v/w)	Hydrodistillation (Clevenger, 3,3 h)	[64]
1st cutting (all irrigation regimes $\times$ 5 nutrient sources combined), 107-day growth period, Afyonkarahisar, Turkey	21.69–27.86%	19.43–24.72%	8.50–12.79%	4.03–8.50%	4.00–6.89%	3.07–5.40%	2.77–5.24%	3.11–7.24%	2.75–4.64%		0.16–2.30%	1.28–1.80% (v/w)	Hydrodistillation (neo-Clevenger, 3 h; 50 g dried leaves/500 mL water)	[65]
2nd cutting (all irrigation regimes $\times$ 5 nutrient sources combined), 72-day growth period, Afyonkarahisar, Turkey	24.40–34.29%	18.18–27.08%	7.91–13.30%	3.95–9.99%	3.51–6.31%	2.27–3.47%	2.28–4.40%	2.79–6.57%	2.76–4.58%		1.76–3.08%	1.07–1.54% (v/w)	Hydrodistillation (neo-Clevenger, 3 h; 50 g dried leaves/500 mL water)	[65]
flowers/leaves/stems	18.17%	1.49%	12.87%		0.69%				1.76%		16.97%	NR	Steam distillation (100°C)	[99]
<i>Mentha piperita</i>	Carvone	D-Limonene	β -Caryophyllene	Eucalyptol	Germacrene D	L-menthol	Menthol	L-menthone	Menthone	1,8-Cineole	1,8-Epoxy-p-menthane	EO Yield	Extraction method	Ref.
compiled ranges; air-dried parts	3.5%	0.6–4.5%		0.4–12%		38–70%		0.4–35%				0.1–1% (general value); widened to 0.5–4% in some reports	Steam distillation; raw oil often redistilled/rectified to remove sulphur compounds	[68]
Midwest USA							38.45%		21.80%	5.62%		NR	NR	[70]
Morocco; irrigated with treated wastewater	51.35%	17.88%	4.39%	10.69%	5.21%							NR	NR	[70]
Morocco; irrigated with well water	76.89%	3.27%	3.02%	5.22%	2.97%							NR	NR	[70]
Morocco; irrigated with river water	77.17%	3.42%	2.93%								5.06%	NR	NR	[70]

Table 2: *Cont.*

<i>Juniperus communis</i>	α -Pinene	Sabinene	Germacrene D	δ -Cadinene	β -Caryophyllene	Limonene	Terpinen-4-ol					EO Yield	Extraction method	Ref.
female plant; Rhodope Mts, Bulgaria	34.91%	9.77%	6.53%	4.36%	2.42%	2.14%	5.15%					1.63% (ClevA)/0.61% (SCom)	Hydrodistillation (Clevenger apparatus—ClevA: 800 mL water, 100 g air-dried leaves, 2 h, 2 reps) vs. semi-commercial steam distillation (SCom: 100 L unit, 20 kg leaves+twigs, 3 h)	[76]
male plant; Rhodope Mts, Bulgaria	26.81%	9.28%	6.87%	6.33%	3.69%	7.22%	3.98%					0.32% (ClevA)/0.24% (SCom)	Hydrodistillation (Clevenger apparatus—ClevA: 800 mL water, 100 g air-dried leaves, 2 h, 2 reps) vs. semi-commercial steam distillation (SCom: 100 L unit, 20 kg leaves+twigs, 3 h)	[76]
needles (top part), wild, Tandi, Lahaul & Spiti, Himachal Pradesh, India; collected July 2015	49.0%	2.5%	0.9%	0.1%		16.6%	0.3%					0.32% (v/w)	Hydrodistillation (Clevenger-type apparatus, 3 h)	[72]
needles (top part), cultivated clone C-1, lower altitude (~1300 m), Palampur, India; collected October 2015	7.2%	40.1%	0.5%	2.2%		0.8%	13.3%					0.34% (v/w)	Hydrodistillation (Clevenger-type apparatus, 3 h)	[72]
needles (top part), cultivated clone C-2, lower altitude (~1300 m), Palampur, India; collected October 2015	6.3%	37.1%	0.6%	1.0%		0.7%	10.2%					0.56% (v/w)	Hydrodistillation (Clevenger-type apparatus, 3 h)	[72]
needles (top part), cultivated clone C-3, lower altitude (~1300 m), Palampur, India; collected October 2015	2.8%	37.0%		2.0%		1.0%	19.5%					0.26% (v/w)	Hydrodistillation (Clevenger-type apparatus, 3 h)	[72]
needles (top part), cultivated clone C-4, lower altitude (~1300 m), Palampur, India; collected October 2015	8.2%	43.3%	0.6%	1.2%		1.3%	13.6%					0.43% (v/w)	Hydrodistillation (Clevenger-type apparatus, 3 h)	[72]
needles (top part), cultivated clone C-5, lower altitude (~1300 m), Palampur, India; collected October 2015	8.5%	47.3%	0.3%	0.5%		1.0%	14.4%					0.34% (v/w)	Hydrodistillation (Clevenger-type apparatus, 3 h)	[72]
needles (top part), cultivated clone C-6, lower altitude (~1300 m), Palampur, India; collected October 2015	19.3%	39.2%		0.1%		1.0%	8.6%					0.42% (v/w)	Hydrodistillation (Clevenger-type apparatus, 3 h)	[72]
needles (top part), cultivated clone C-7, lower altitude (~1300 m), Palampur, India; collected October 2015	41.3%	0.4%	0.1%	1.9%		32.8%	0.4%					0.43% (v/w)	Hydrodistillation (Clevenger-type apparatus, 3 h)	[72]
<i>Rosmarinus officinalis</i>	1,8-Cineole	α -Pinene	Camphor	Limonene	Camphene	β -Myrcene	p-Cymene	α -Terpineol	β -pinene	α -Terpinene	Borneol	EO Yield	Extraction method	Ref.
leaves; Boulemane/Skoura, Morocco	40.80%	26.18%	19.53%	2.71%	2.23%	2.11%	1.30%	1.26%	0.39%	0.53%	0.52%	2.44% (v/w)	Hydrodistillation (Clevenger-type apparatus, 200 g dried material, 1000 mL distilled water, 3 h)	[82]
commercial oil, Sichuan Province, China	27.23%	19.43%	14.26%		11.52%				6.71%			NR	Steam distillation	[104]

NR = not reported; v/w = oil volume per plant weight (v/w); w/w = oil mass per raw material mass; $\pm$ = standard deviation; ClevA = Clevenger apparatus (academic-scale hydrodistillation); SCom = semi-commercial steam distillation; cv. = cultivar; PA = Pará (Brazil); MA = Maranhão (Brazil); Blank cells indicate that the corresponding compound was not reported for that sample by the cited source, not that it is absent from the essential oil.



Figure 1: Heatmap of essential oil compound profiles across the plant samples and populations discussed in this review. Color scale: white = low reported percentage (near 0%); intense red = high reported percentage; gray cells = compound not reported for that sample by the cited source (not necessarily absent from the essential oil). Labels containing “(range)” indicate the source reported compound concentrations as a range rather than single values; the color shown reflects the midpoint (mean) of that range. Abbreviations in sample labels: cv. = cultivar; C-1 to C-7 = cultivated clonal lines; #1/#2 = two distinct chemotype samples reported from the same collection site; PA = par  (Brazil); MA = maranh o (Brazil).

Across the plant species and populations analyzed, the predominant method used for essential oil extraction was hydrodistillation (Fig. 2). The highest yield was recorded for *Zingiber zerumbet* (5.0%, hydrodistillation), followed by *Levisticum officinale* (2.8%, hydrodistillation), while the lowest yield was reported for *Spilanthes paniculata* roots (0.03%, hydrodistillation). Considerable variability in yield obtained by the same extraction method (hydrodistillation) was observed within the same species, depending on origin/habitat—for example, *Thymus serpyllum* ranged from 0.4% to 1.4%, highlighting the strong influence of growing conditions on essential oil content (Fig. 2, Table 2). Furthermore, when comparing extraction methods on the same samples, hydrodistillation consistently produced higher yields than semi-commercial steam distillation in *Juniperus communis* (1.63% versus 0.61% in female plants; 0.32% versus 0.24% in male plants; Fig. 2, Table 2).



Figure 2: Essential oil yield (%) reported for the plant samples discussed in this review, by extraction method. Bar color = extraction method: blue = hydrodistillation (Clevenger); red = steam distillation; green = steam distillation (semi-commercial). Labels ending in “(range)” indicate the source reported a yield range; the bar shows the midpoint (mean) of that range. Abbreviations: cv. = cultivar; C-1 to C-7 = cultivated clonal lines; #1/#2 = two distinct samples from the same site; PA = Pará (Brazil); MA = Maranhão (Brazil).

4 From Plant Ecological Functions to Antitumoral Activity in OSCC Models

The antimicrobial activity of essential oils is primarily attributed to their lipophilic nature, which allows their constituents to penetrate microbial cell walls and cytoplasmic membranes, thereby increasing membrane permeability and causing leakage of intracellular components, ions, and ATP [106]. This membrane disruption is accompanied by impairment of membrane proteins, reduction of membrane potential and proton motive force, and interference with cellular respiration and energy production, ultimately compromising essential cellular functions [106,107]. Beyond these core membrane-targeting effects, essential oils have also been reported to inhibit biofilm formation and efflux pumps, induce reactive oxygen species (ROS) generation, disrupt mitochondrial function, and interfere with DNA and protein synthesis; in fungal cells, they may additionally arrest the cell cycle and induce apoptosis [107]. Collectively, these multiple and often overlapping mechanisms lead to loss of cellular integrity, metabolic dysfunction, growth inhibition, and ultimately microbial cell death. In phytopathogenic fungi specifically, essential oil exposure has been associated with loss of membrane integrity, mitochondrial impairment, and reduced ATP production, mechanisms that parallel those described in human-pathogen models [108]. Notably, several of these same processes—membrane disruption, mitochondrial dysfunction, and ROS-mediated damage—recur as central mechanisms in the cytotoxic activity of essential oils against OSCC cells, suggesting a possible mechanistic continuity between their antimicrobial and antitumoral effects.

Across the diverse plant taxa analyzed in this review, including members of the Lamiaceae (e.g., *Thymus*, *Salvia*, *Mentha*, *Rosmarinus*), Lauraceae (*Cinnamomum*), Piperaceae (*Piper*), Zingiberaceae (*Zingiber*), Apiaceae (*Levisticum*), Asteraceae (*Spilanthes*), Scrophulariaceae (*Scrophularia*), and Cupressaceae (*Juniperus*), a consistent pattern emerges linking taxonomic diversity, organ-specific essential oil accumulation, and ecological function with the observed cytotoxic activity in OSCC models. Despite their phylogenetic distance, these taxa converge functionally in producing volatile secondary metabolites, predominantly monoterpenes, sesquiterpenes, phenylpropanoids, and oxygenated derivatives, which are differentially accumulated in specialized secretory structures such as glandular trichomes, secretory ducts, rhizomes, bark, or leaves. From an ecological perspective, these compounds primarily function as multifunctional chemical defense agents, mediating plant–environment interactions through protection against herbivores, microbial pathogens, and competing vegetation, while also contributing to pollinator attraction and abiotic stress adaptation. This ecological role is particularly evident in the strong antimicrobial, insecticidal, antifungal, and allelopathic activities consistently reported across species, reflecting their importance in plant survival and fitness across diverse habitats and environmental gradients.

Mechanistically, several classes of compounds that confer ecological advantages *in planta*—including thymol, carvacrol, cinnamaldehyde, eugenol, β -pinene, zerumbone, ligustilide, menthol, and camphor—also exhibit pronounced bioactivity against OSCC cells, inducing apoptosis, cell cycle arrest, and disruption of mitochondrial and membrane integrity, as detailed for each species in Section 3. Molecular targets identified across these models include p53, NF- κ B, and caspase-dependent signaling pathways. These effects may be interpreted as an extension of the original ecological function of these metabolites as broad-spectrum cytotoxic and stress-inducing agents in biological antagonists. Accordingly, the antitumoral activity observed in OSCC models may be interpreted, at least in part, as a translational manifestation of evolutionarily conserved chemical defense strategies in plants. As shown in Table 2, this mechanistic continuity is well supported for some species (e.g., *Thymus*, *Cinnamomum*, *Piper*, *Zingiber*, *Mentha*), while for others it remains unconfirmed or only weakly analogous. This integrative perspective highlights essential oils as ecologically shaped metabolite systems in which phylogenetic background, organ specialization, and

environmental pressures collectively determine chemical diversity, which in turn underlies their secondary pharmacological relevance in human cancer models.

As summarized in Table 3, the ecological functions of essential oil constituents provide a conceptual framework for interpreting their reported antitumoral activities in OSCC models. Although direct evolutionary or mechanistic relationships remain to be experimentally established, the convergence of ecological defense functions and anticancer bioactivities supports the hypothesis that these properties may arise from conserved biological activities of plant secondary metabolites.

These convergences, chemical (Fig. 1), functional, and mechanistic, indicate that a shared terpenoid biosynthetic background, rather than phylogenetic relatedness, is the more plausible basis for the ecological–anticancer relationship proposed in this review.

Beyond this conceptual convergence, translational relevance is also constrained by the pharmacokinetic behavior of these constituents. Eugenol and cinnamaldehyde show poor oral bioavailability in rats, at $4.25 \pm 0.11\%$ and $7.33 \pm 0.37\%$, respectively [109]. Thymol's oral bioavailability in humans, measured as thymol sulfate, is about 16% [110]. More broadly, eugenol, thymol, cinnamaldehyde and carvacrol display limited bioavailability due to restricted intestinal absorption and rapid metabolism—mainly glucuronidation and sulfation, or oxidation in the case of aldehydes [111]. Eugenol and cinnamaldehyde also show dose-dependent cytotoxic effects on mammalian cells and organs such as the liver [111]. Clinical translation of these compounds would require targeted delivery systems that maximize local exposure while avoiding systemic peaks, or synergistic strategies allowing dose reduction [111].

Table 3: Representative essential oil-producing plant species evaluated in OSCC models, their major bioactive constituents, ecological functions, reported antitumoral activities, and the proposed ecological basis for these effects.

No.	Species	Major EO Constituents	EO Mechanism against Pathogens	EO Mechanism against OSCC	Potential Ecological–Anticancer Relationship	References
1	<i>Thymus vulgaris</i>	Thymol, carvacrol (chemotype-dependent); p-cymene	Membrane disruption, ↑permeability, cytoplasmic leakage (carvacrol); autolysis, biofilm suppression, ergosterol targeting (thymol)	$\Delta\Psi_m$ depolarization, TRPA1-independent apoptosis (thymol; Cal27/SCC4/SCC9)	Both compounds act primarily through membrane/mitochondrial disruption in microorganisms and OSCC cells, suggesting a shared structural target underlying both defensive and antitumoral effects	[10,11,13,29,87]
2	<i>Cinnamomum</i> spp.	Cinnamaldehyde, eugenol (benzyl benzoate, cinnamyl acetate)	Membrane disruption, enzymatic interference, redox imbalance (cinnamaldehyde); antimicrobial/antifungal effects enhanced by eugenol	Apoptosis, ↓EGFR signaling (cinnamaldehyde/cinnamon EO); apoptosis (↑Bax/Bad), ↓MMP-2/9, MIF targeting, G0/G1 arrest (p21/p27/cyclin D1, p53-independent), ↓P38/STAT5/NF-κB (eugenol)	Membrane disruption and redox/enzymatic interference documented against pathogens parallel the apoptotic and cell-cycle effects of the same constituents (cinnamaldehyde, eugenol) in OSCC cells	[15,33–35,89,90,92,93]
3	<i>Piper rivinoides</i>	α-Pinene, β-pinene (limonene)	Antibacterial (Gram+/-), antifungal vs. <i>Candida</i> spp. (α-/β-pinene)	Caspase-dependent apoptosis (membrane blebbing, nuclear pyknosis); enriched fraction more selective than carboplatin	The same monoterpenes (α-/β-pinene) associated with antimicrobial defense also drive caspase-mediated apoptosis in OSCC	[16,36,37]

Table 3: Cont.

No.	Species	Major EO Constituents	EO Mechanism against Pathogens	EO Mechanism against OSCC	Potential Ecological–Anticancer Relationship	References
4	<i>Zingiber zerumbet</i>	Zerumbone (rhizome), humulene, β -caryophyllene; nerolidol/linalool/pinenes (aerial parts)	Membrane disruption; leakage of proteins, nucleic acids, ATP (zerumbone)	Intrinsic/extrinsic apoptosis, S/G2-M arrest; IC ₅₀ 1.93/1.13 μ g/mL (H103/ORL-204)	Zerumbone's membrane-disruptive antimicrobial action is paralleled by its apoptosis-inducing activity in OSCC cells	[18,39,44]
5	<i>Levisticum officinale</i>	Monoterpenes, phthalides ((Z)-ligustilide, neocnidilide), α -terpinyl acetate, β -phellandrene	InhA inhibition (mycobacterial cell wall biosynthesis); affinity $\geq$ isoniazid	Modulation of ERK5, ILK, p53 signaling; apoptosis-/cell cycle-related gene effects (IC ₅₀ 292.6 μ g/mL; UMSCC1)	Compounds interfering with cell wall/membrane-related targets in pathogens also modulate proliferation- and apoptosis-related signaling in OSCC	[18,47,48]
6	<i>Spilanthes paniculata</i>	Spathulenol, germacrene D, (E)-caryophyllene, δ -amorphene, β -bisabolene, limonene	Membrane disruption (Gram+ > Gram–); larvicidal/insecticidal (spilanthalol); dose-dependent antifungal activity	Early apoptosis (2.5 $\times$ > leaf EO); p53 binding (spathulenol); IC ₅₀ 113.95 μ g/mL	Membrane-interacting/neurotoxic mechanisms against pathogens and insects are mirrored by spathulenol's proposed p53-mediated apoptotic action in OSCC	[20,53–56]
7	<i>Scrophularia oxysepala</i>	Phytol, methyl benzyl alcohol, dehydrodieugenol, eugenol	Insecticidal (acylated iridoids); free-radical scavenging	Apoptosis via $\uparrow$ BAX/SMAC, $\downarrow$ BCL2/SURVIVIN (OECM-1)	Oxidative-stress-related defense compounds (iridoids, phenolics) are associated with apoptosis-regulating gene modulation in OSCC	[21,59]
8	<i>Salvia officinalis</i>	α -/ β -Thujone, camphor, 1,8-cineole, rosmarinic acid, carnosic acid, carnosol	Bactericidal/bacteriostatic, antifungal/antiviral (diterpenes); insecticidal, allelopathic; $\uparrow$ EO under drought	Biphasic effect; cytotoxicity above IC ₅₀ 135 μ g/mL via AhR signaling, G1/S checkpoint, p53 signaling (UMSCC1)	The same terpenoid/diterpene constituents responsible for antimicrobial defense are implicated in multi-pathway antiproliferative signaling in OSCC	[61,65–68,98]
9	<i>Mentha piperita</i>	Menthol, menthone, limonene, linalool, pulegone, 1,8-cineole	Antibacterial (Gram+ > Gram–); biofilm inhibition ($\downarrow$ glycosyltransferase genes)	Dose-dependent cytotoxicity, apoptosis-like morphology (OSCC-related models)	Membrane/biofilm-disrupting antimicrobial mechanisms parallel the cytotoxic/apoptotic damage observed in tumor cells	[14,70,72,100]
10	<i>Juniperus</i> spp.	α -Pinene, sabinene, β -pinene, limonene, β -myrcene, β -caryophyllene, germacrene D	Repellent/insecticidal (aphids); antifungal vs. <i>Fusarium</i> , <i>Rhizoctonia</i> , <i>Cylindrocarpon</i> spp.	$\downarrow$ Viability (SCC-25, dose-dependent); G0/G1 arrest (p53/p21, Rb), intrinsic/extrinsic apoptosis (OECM-1); synergistic with 5-FU	Antimicrobial/insecticidal activity is well documented, and direct mechanistic evidence of cell-cycle arrest and apoptosis in OSCC has been reported, although whether the same terpenoid constituents underlie both defensive and antitumoral effects remains to be confirmed	[14,78,102]
11	<i>Rosmarinus officinalis</i>	1,8-Cineole, α -pinene, camphor, camphene, β -pinene	Synergistic antifungal (complete inhibition of <i>B. cinerea</i>); insecticidal (acetylcholinesterase, β -tubulin)	$\downarrow$ Viability (SCC-25, primary cultures), dose-dependent; mechanism unconfirmed	Antimicrobial/insecticidal synergy is well documented, but the anticancer effect in OSCC is limited to antiproliferative observations without a confirmed mechanism	[14,84–86,104]

5 Conclusions

This review highlights that essential oils from phylogenetically diverse plant species share common chemical and biological features that may be relevant for oral squamous cell carcinoma (OSCC). Major constituents, including thymol, carvacrol, eugenol, cinnamaldehyde, α -pinene, β -pinene, and zerumbone, predominantly exhibit antiproliferative and pro-apoptotic activities, with several species also showing anti-migratory effects and modulation of cell-cycle progression, oxidative stress, and cancer-related signaling pathways. By integrating botanical classification, organ-specific accumulation of essential oils, ecological functions, and experimental evidence from OSCC models, this review proposes that the anticancer activities of these metabolites may reflect, at least in part, biochemical properties originally evolved for plant defense and adaptation to biotic and abiotic stress. Although this ecological–anticancer relationship remains a conceptual framework requiring further experimental validation, it offers a broader perspective for interpreting the pharmacological potential of essential oils. Future studies should focus on standardization of essential oil composition, mechanistic validation, and well-designed preclinical and clinical investigations to facilitate the development of essential oil-derived compounds as complementary therapeutic strategies for OSCC.

Acknowledgement: Not applicable.

Funding Statement: The authors received no specific funding for this study.

Author Contributions: The authors confirm contribution to the paper as follows: study conception and design: Bianca Voicu Balasea; data collection: Melis Izet, Florentina Rus, and Ana Cernega; analysis and interpretation of results: Bianca Voicu Balasea, Cristina Neculau and Alexandra Popa; draft manuscript preparation: Bianca Voicu Balasea; review of results: Cristina Neculau, Alexandra Popa, Alexandra Ripszky and Simona Parvu; approval of the final version of the manuscript: Alexandra Ripszky and Simona Parvu. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials: The authors confirm that the data supporting the findings of this study are available within the article and its Supplementary Materials.

Ethics Approval: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

Supplementary Materials: The supplementary material is available online at <https://www.techscience.com/doi/10.32604/phyton.2026.088883/s1>.

References

1. Feng Z, Bartholomew ES, Liu Z, Cui Y, Dong Y, Li S, et al. Glandular trichomes: New focus on horticultural crops. *Hortic Res.* 2021;8(1):158. [[CrossRef](#)].
2. Dötterl S, Gershenzon J. Chemistry, biosynthesis and biology of floral volatiles: Roles in pollination and other functions. *Nat Prod Rep.* 2023;40(12):1901–37. [[CrossRef](#)].
3. Gostin IN, Blidar CF. Glandular trichomes and essential oils variability in species of the genus *Phlomis* L.: A review. *Plants.* 2024;13(10):1338. [[CrossRef](#)].
4. War AR, Paulraj MG, Ahmad T, Buhroo AA, Hussain B, Ignacimuthu S, et al. Mechanisms of plant defense against insect herbivores. *Plant Signal Behav.* 2012;7(10):1306–20. [[CrossRef](#)].
5. Borromeo I, Giordani C, Forni C. The role of plant-derived essential oils in eco-friendly crop protection strategies under drought and salt stress. *Plants.* 2025;14(24):3789. [[CrossRef](#)].

6. Spigarelli R, Valerii MC, Bernacchi A, Dussias NK, Mbirki L, Spisni E. Essential oils as a source of anticancer molecules: Critical assessment of current evidence and methodological limitations—A systematic review. *Int J Mol Sci.* 2026;27(10):4379. [[CrossRef](#)].
7. Dhifi W, Bellili S, Jazi S, Bahloul N, Mnif W. Essential oils' chemical characterization and investigation of some biological activities: A critical review. *Medicines.* 2016;3(4):25. [[CrossRef](#)].
8. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209–49. [[CrossRef](#)].
9. Dai W, Sun C, Huang S, Zhou Q. Carvacrol suppresses proliferation and invasion in human oral squamous cell carcinoma. *Onco Targets Ther.* 2016;9:2297–304. [[CrossRef](#)].
10. De La Chapa JJ, Singha PK, Lee DR, Gonzales CB. Thymol inhibits oral squamous cell carcinoma growth via mitochondria-mediated apoptosis. *J Oral Pathol Med.* 2018;47(7):674–82. [[CrossRef](#)].
11. Monith Raj G, David Wilson D, Jenitha V, Kokelavani NB, Vijay N, Srividhya M, et al. Human cell toxicity and *in vivo* bioavailability of therapeutic essential oils—A review. *Fitoterapia.* 2025;186:106801. [[CrossRef](#)].
12. Sertel S, Eichhorn T, Plinkert PK, Efferth T. Cytotoxicity of *Thymus vulgaris* essential oil towards human oral cavity squamous cell carcinoma. *Anticancer Res.* 2011;31(1):81–7.
13. Lazarević M, Milošević M, Petrović N, Petrović S, Damante G, Milašin J, et al. Cytotoxic effects of different aromatic plants essential oils on oral squamous cell carcinoma: An *in vitro* study. *Balkan J Dent Med.* 2019;23(3):73–9. [[CrossRef](#)].
14. Ahmed B, Abdel ghani S. Effect of cinnamon oil and scorpion venom on oral squamous cell carcinoma cell line (*In vitro* study). *Egypt Dent J.* 2022;68(1):533–41. [[CrossRef](#)].
15. Machado TQ, Felisberto JRS, Guimarães EF, Queiroz GA, Fonseca ACCD, Ramos YJ, et al. Apoptotic effect of β -pinene on oral squamous cell carcinoma as one of the major compounds from essential oil of medicinal plant *Piper rivinoides* Kunth. *Nat Prod Res.* 2022;36(6):1636–40. [[CrossRef](#)].
16. Fonseca ACCD, de Queiroz LN, Sales Felisberto J, Jessé Ramos Y, Mesquita Marques A, Wermelinger GF, et al. Cytotoxic effect of pure compounds from *Piper rivinoides* Kunth against oral squamous cell carcinoma. *Nat Prod Res.* 2021;35(24):6163–7. [[CrossRef](#)].
17. Amil MA, Sim KS, Mohd Asngari NJ, Mohd Bakri M, Abdul Razak F, Yap LF, et al. Evaluation of the antiproliferative effect of *Zingiber zerumbet* essential oil against oral squamous cell carcinoma. *S Afr N J Bot.* 2025;187:337–50. [[CrossRef](#)].
18. Sertel S, Eichhorn T, Plinkert PK, Efferth T. Chemical composition and antiproliferative activity of essential oil from the leaves of a medicinal herb, *Levisticum officinale*, against UMSCC1 head and neck squamous carcinoma cells. *Anticancer Res.* 2011;31(1):185–91.
19. Satapathy SS, Bhuyan R, Pradhan AK, Satpathy S, Panda NR, Bhuyan SK. Comparative evaluation of anticancer potential of *Spilanthes paniculata* leaf and flower essential oil using annexin V and orosphere formation in oral cancer cell line. *Med Oncol.* 2024;41(11):259. [[CrossRef](#)].
20. Totmaj MA, Dadelahi S, Varmazyar S, Abbasi M. *Scrophularia oxysepala* inhibit oral cancer cell line OECM-1 through induction of apoptosis. *Hum Gene.* 2022;34:201080. [[CrossRef](#)].
21. Vouillamoz JF, Christ B. *Thymus vulgaris* L.: Thyme. In: Medicinal, aromatic and stimulant plants. Cham, Switzerland: Springer International Publishing; 2020. p. 547–57. [[CrossRef](#)].
22. Trendafilova A, Todorova M, Ivanova V, Zhelev P, Aneva I. Essential oil composition of ten species from sect. Serpyllum of genus thymus growing in *Bulgaria*. *Diversity.* 2023;15(6):759. [[CrossRef](#)].
23. Salehi B, Mishra AP, Shukla I, Sharifi-Rad M, Contreras MDM, Segura-Carretero A, et al. Thymol, thyme, and other plant sources: Health and potential uses. *Phytother Res.* 2018;32(9):1688–706. [[CrossRef](#)].
24. Kryvtsova M, Hrytsyna M, Salamon I, Skybitska M, Novykevych O. Chemotypes of species of the genus thymus L. in carpathians region of Ukraine—Their essential oil qualitative and quantitative characteristics and antimicrobial activity. *Horticultrae.* 2022;8(12):1218. [[CrossRef](#)].
25. Lazarević J, Jevremović S, Kostić I, Kostić M, Vuleta A, Manitašević Jovanović S, et al. Toxic, oviposition deterrent and oxidative stress effects of *Thymus vulgaris* essential oil against *Acanthoscelides obtectus*. *Insects.* 2020;11(9):563. [[CrossRef](#)].

26. Salaria D, Rolta R, Lal UR, Dev K, Kumar V. A comprehensive review on traditional applications, phytochemistry, pharmacology, and toxicology of *Thymus serpyllum*. Indian J Pharmacol. 2023;55(6):385–94. [\[CrossRef\]](#).
27. Kosakowska O, Węglarz Z, Styczyńska S, Synowiec A, Gniewosz M, Bączek K. Activity of common thyme (*Thymus vulgaris* L.), Greek oregano (*Origanum vulgare* L. ssp. *hirtum*), and common oregano (*Origanum vulgare* L. ssp. *vulgare*) essential oils against selected phytopathogens. Molecules. 2024;29(19):4617. [\[CrossRef\]](#).
28. Vassiliou E, Awolaye O, Davis A, Mishra S. Anti-inflammatory and antimicrobial properties of thyme oil and its main constituents. Int J Mol Sci. 2023;24(8):6936. [\[CrossRef\]](#).
29. Xavier JKAM, Baia TGC, Alegria OVC, Figueiredo PLB, Carneiro AR, Moreira ECO, et al. Essential oil chemotypes and genetic variability of *Cinnamomum verum* leaf samples commercialized and cultivated in the Amazon. Molecules. 2022;27(21):7337. [\[CrossRef\]](#).
30. Yang Z, Liu B, Yang Y, Ferguson DK. Phylogeny and taxonomy of *Cinnamomum* (Lauraceae). Ecol Evol. 2022;12(10):e9378. [\[CrossRef\]](#).
31. Huang Y, Wang W, Xin X, Yang S, Bai W, Zhao W, et al. Compounds of essential oils from different parts of *Cinnamomum cassia* and the perception mechanism of their characteristic flavors. Foods. 2025;14(20):3570. [\[CrossRef\]](#).
32. Gębarowska E, Budek K, Gębarowska M, Kmiec A, Szumny A. Cinnamon bark essential oil as a natural plant protection agent: Chemical profile, antimicrobial activity, and defence induction. Molecules. 2026;31(6):1036. [\[CrossRef\]](#).
33. Guo J, Jiang X, Tian Y, Yan S, Liu J, Xie J, et al. Therapeutic potential of cinnamon oil: Chemical composition, pharmacological actions, and applications. Pharmaceuticals. 2024;17(12):1700. [\[CrossRef\]](#).
34. Yursida Y, Andrew F, Agustina K, Mareza E, Kalsum U, Ikhwan I, et al. Harnessing the power of cinnamon oil: A review of its potential as natural biopesticide and its implications for food security. Heliyon. 2025;11(2):e41827. [\[CrossRef\]](#).
35. da Silva JK, da Trindade R, Alves NS, Figueiredo PL, Maia JGS, Setzer WN. Essential oils from neotropical *Piper* species and their biological activities. Int J Mol Sci. 2017;18(12):2571. [\[CrossRef\]](#).
36. Felisberto JS, Fagundes TF, Oliveira-Souza L, de Souza BHG, de Brito DM, Assunção JA, et al. Organ-specific distribution of antimycobacterial neolignans in *Piper rivinoides* and UHPLC-HRMS/MS analysis of its extracts. Molecules. 2025;30(24):4682. [\[CrossRef\]](#).
37. Felisberto JS, Machado DB, Assunção JAS, Massau SAS, Queiroz GA, Guimarães EF, et al. Spatio-temporal variations of volatile metabolites as an eco-physiological response of a native species in the tropical forest. Plants. 2024;13(18):2599. [\[CrossRef\]](#).
38. Padalia RC, Verma RS, Chauhan A, Singh VR, Goswami P, Singh S, et al. *Zingiber zerumbet* (L.) Roscoe ex Sm. from northern India: Potential source of zerumbone rich essential oil for antiproliferative and antibacterial applications. Ind Crops Prod. 2018;112:749–54. [\[CrossRef\]](#).
39. Li DM, Ye YJ, Xu YC, Liu JM, Zhu GF. Complete chloroplast genomes of *Zingiber montanum* and *Zingiber zerumbet*: Genome structure, comparative and phylogenetic analyses. PLoS One. 2020;15(7):e0236590. [\[CrossRef\]](#).
40. Thakur N, Kaur J, Aakriti, Thakur C. *Zingiber zerumbet* (shampoo ginger). In: Underutilized tuber crops of the himalayan region. Amsterdam, The Netherlands: Elsevier; 2026. p. 593–617. [\[CrossRef\]](#).
41. Sapkal A, Attar S, Chavan J, Kumbhar A, Kamble S. *Zingiber zerumbet*: A green and ecofriendly natural surfactant for the synthesis of bis(indolyl)methane, tris-indoline and spirooxindole derivatives. Sustain Chem Pharm. 2023;35:101228. [\[CrossRef\]](#).
42. Moreira da Silva T, Pinheiro CD, Puccinelli Orlandi P, Pinheiro CC, Soares Pontes G. Zerumbone from *Zingiber zerumbet* (L.) Smith: A potential prophylactic and therapeutic agent against the cariogenic bacterium *Streptococcus mutans*. BMC Complement Altern Med. 2018;18(1):301. [\[CrossRef\]](#).
43. Zhang C, Xie Y, Qiu W, Mei J, Xie J. Antibacterial and antibiofilm efficacy and mechanism of ginger (*Zingiber officinale*) essential oil against *Shewanella putrefaciens*. Plants. 2023;12(8):1720. [\[CrossRef\]](#).
44. Złotek U, Szymanowska U, Pecio Ł, Kozachok S, Jakubczyk A. Antioxidative and potentially anti-inflammatory activity of phenolics from lovage leaves *Levisticum officinale* Koch elicited with jasmonic acid and yeast extract. Molecules. 2019;24(7):1441. [\[CrossRef\]](#).
45. Olennikov DN. Coumarins of lovage roots (*Levisticum officinale* W.D.J.Koch): LC-MS profile, quantification, and stability during postharvest storage. Metabolites. 2022;13(1):3. [\[CrossRef\]](#).

46. Luiz Soares Basilio DC, de Moraes Berenguel Lossavaro PK, Espinoça IT, Coronel PMV, dos Santos Lencina J, Lucier OL, et al. *Levisticum officinale* essential oil prevents paracetamol-induced hepatotoxicity by decreasing oxidative stress. *PharmaNutrition*. 2026;36:100469. [\[CrossRef\]](#).
47. Sahlabgi A, Lupuliasa D, Stoicescu I, Vlaia LL, Licu M, Popescu A, et al. Determination of the phytochemical profile and antioxidant activity of some alcoholic extracts of *Levisticum officinale* with pharmaceutical and cosmetic applications. *Separations*. 2025;12(4):79. [\[CrossRef\]](#).
48. Miran M, Feizabadi MM, Kazemian H, Kardan-Yamchi J, Monsef-Esfahani HR, Ebrahimi SN. The activity of *Levisticum officinale* W.D.J. Koch essential oil against multidrug-resistant *Mycobacterium tuberculosis*. *Iran J Microbiol*. 2018;10(6):394.
49. Paulraj J, Govindarajan R, Palpu P. The Genus *Spilanthes* ethnopharmacology, phytochemistry, and pharmacological properties: A review. *Adv Pharmacol Sci*. 2013;2013:510298. [\[CrossRef\]](#).
50. Panyadee P, Inta A. Taxonomy and ethnobotany of *Acmella* (Asteraceae) in Thailand. *Biodiversitas*. 2022;23(4):2177–86. [\[CrossRef\]](#).
51. Satapathy SS, Bhuyan R, Sahoo A, Sahoo C, Bhuyan SK. Phytochemical profiling of all parts of *Spilanthes paniculata* (Toothache plant) for therapeutic implications. *Res J Biotech*. 2024;19(12):79. [\[CrossRef\]](#).
52. Dubey S, Maity S, Singh M, Saraf SA, Saha S. Phytochemistry, pharmacology and toxicology of *Spilanthes acmella*: A review. *Adv Pharmacol Sci*. 2013;2013:423750. [\[CrossRef\]](#).
53. Sharma R, Arumugam N. N-alkylamides of *Spilanthes* (syn: *Acmella*): Structure, purification, characterization, biological activities and applications—A review. *Future Foods*. 2021;3:100022. [\[CrossRef\]](#).
54. Zhu SM, Zhu L, Tian YJ, Yin YC. Composition and antimicrobial activity of the essential oil of *Spilanthes paniculata* growing wild on the gaoligong mountains, China. *Asian J Chem*. 2012;24(2):607–10.
55. Scheunert A. Evolutionary history and biogeography of the genus *Scrophularia* (Scrophulariaceae) and hemiparasitic Orobanchaceae (tribe Rhinanthaeae) with emphasis on reticulate evolution [dissertation]. Munich, Germany: LMU; 2017.
56. Tojibaev KS, Khassanov FO, Beshko NY, Tajetdinova DM, Turginov OT, Sennikov AN, et al. Diversity and distribution of the genus *Scrophularia* L. (Scrophulariaceae) in Uzbekistan. *J Asia Pac Biodivers*. 2020;13(1):70–91. [\[CrossRef\]](#).
57. Pasdaran A, Delazar A, Ayatollahi SA, Pasdaran A. Chemical composition and biological activities of methanolic extract of *Scrophularia oxysepala* boiss. *Iran J Pharm Res*. 2017;16(1):338–46.
58. Nicolescu A, Frumuzachi O, Mocan A. Ethnobotanical diversity of the genus *Salvia* L. (Lamiaceae): From medicinal and culinary applications to cultural importance of sage species across the globe. *J Ethnopharmacol*. 2026;359:121049. [\[CrossRef\]](#).
59. Anjali, Garg D, Pragi, Kumar V, Dimple, Monika. A review of therapeutic properties and uses of *Salvia officinalis*. *J Pharma Insights Res*. 2024;2(3):146–54. [\[CrossRef\]](#).
60. Kalnyuk JV, Yurkevich OY, Badaeva ED, Semenov AR, Zoshchuk SA, Amosova AV, et al. Taxonomy, phylogeny, genomes, and repeatomes in the subgenera *Salvia*, *Sclarea*, and *Glutinaria* (*Salvia*, Lamiaceae). *Int J Mol Sci*. 2025;26(13):6436. [\[CrossRef\]](#).
61. Radosavljević I, Satovic Z, di Pietro R, Jug Dujaković M, Varga F, Škrčić D, et al. Phylogeographic structure of common sage (*Salvia officinalis* L.) reveals microrefugia throughout the Balkans and colonizations of the Apennines. *Sci Rep*. 2022;12(1):15726. [\[CrossRef\]](#).
62. Jažo Z, Glumac M, Paštar V, Bektić S, Radan M, Carev I. Chemical composition and biological activity of *Salvia officinalis* L. essential oil. *Plants*. 2023;12(9):1794. [\[CrossRef\]](#).
63. Cutillas AB, Carrasco A, Martinez-Gutierrez R, Tomas V, Tudela J. *Salvia officinalis* L. essential oils from Spain: Determination of composition, antioxidant capacity, antienzymatic, and antimicrobial bioactivities. *Chem Biodivers*. 2017;14(8):e1700102. [\[CrossRef\]](#).
64. Khedher MRB, Khedher SB, Chaieb I, Tounsi S, Hammami M. Chemical composition and biological activities of *Salvia officinalis* essential oil from Tunisia. *EXCLI J*. 2017;16:160–73. [\[CrossRef\]](#).
65. Soltanbeigi A, Yıldız M, Diraman H, Terzi H, Sakartepe E, Yıldız E. Growth responses and essential oil profile of *Salvia officinalis* L. Influenced by water deficit and various nutrient sources in the greenhouse. *Saudi J Biol Sci*. 2021;28(12):7327–35. [\[CrossRef\]](#).

66. Ghorbani A, Esmaeilizadeh M. Pharmacological properties of *Salvia officinalis* and its components. *J Tradit Complement Med.* 2017;7(4):433–40. [[CrossRef](#)].
67. Šarić-Kundalić B, Fialová S, Dobeš C, ŮLZANT S, Tekelová D, Grančai D, et al. Multivariate Numerical Taxonomy of *Mentha* Species, Hybrids, Varieties and Cultivars. *Sci Pharm.* 2009;77(4):851–76. [[CrossRef](#)].
68. Hudz N, Kobylinska L, Pokajewicz K, Horčínová Sedláčková V, Fedin R, Voloshyn M, et al. *Mentha piperita*: Essential oil and extracts, their biological activities, and perspectives on the development of new medicinal and cosmetic products. *Molecules.* 2023;28(21):7444. [[CrossRef](#)].
69. Rios-Esteva R, Turner GW, Lee JM, Croteau RB, Lange BM. A systems biology approach identifies the biochemical mechanisms regulating monoterpenoid essential oil composition in peppermint. *Proc Natl Acad Sci U S A.* 2008;105(8):2818–23. [[CrossRef](#)].
70. Yu Y, Ma Y, Ouyang Z, Huang L. *Mentha* essential oils: Unraveling chemotype-dependent biosynthesis and assessing evidence for health-promoting activities. *Nutrients.* 2025;17(20):3258. [[CrossRef](#)].
71. Soltanbeigi A, Özgüven M, Hassanpouraghdam MB. Planting-date and cutting-time affect the growth and essential oil composition of *Mentha* × *piperita* and *Mentha arvensis*. *Ind Crops Prod.* 2021;170:113790. [[CrossRef](#)].
72. Maurya AK, Devi R, Kumar A, Koundal R, Thakur S, Sharma A, et al. Chemical composition, cytotoxic and antibacterial activities of essential oils of cultivated clones of *Juniperus communis* and wild *Juniperus* species. *Chem Biodivers.* 2018;15(9):e1800183. [[CrossRef](#)].
73. Radoukova T, Semerdjieva I, Zheljaskov VD. A comparative morphological and anatomical study of *Juniperus communis* L., *J. sibirica* burgsd., and *J. pygmaea* K. Koch from *Bulgaria*. *Plants.* 2024;13(17):2419. [[CrossRef](#)].
74. Gutiérrez-Larruscain D, Vargas P, Fernández-Mazuecos M, Pausas JG. Phylogenomic analysis reveals the evolutionary history of Palearctic needle-leaved junipers. *Mol Phylogenet Evol.* 2024;199:108162. [[CrossRef](#)].
75. Ložienė K, Venskutonis PR. Juniper (*Juniperus communis* L.) oils. In: *Essential oils in food preservation, flavor and safety*. Amsterdam, The Netherlands: Academic Press; 2016. p. 495–500. [[CrossRef](#)].
76. Semerdjieva I, Zheljaskov VD, Radoukova T, Dincheva I, Piperkova N, Maneva V, et al. Biological activity of essential oils of four juniper species and their potential as biopesticides. *Molecules.* 2021;26(21):6358. [[CrossRef](#)].
77. Hammer M, Junghanns W. *Rosmarinus officinalis* L.: Rosemary. In: *Medicinal, aromatic and stimulant plants*. Cham, Switzerland: Springer International Publishing; 2020. p. 501–21. [[CrossRef](#)].
78. González-Minero FJ, Bravo-Díaz L, Ayala-Gómez A. *Rosmarinus officinalis* L. (rosemary): An ancient plant with uses in personal healthcare and cosmetics. *Cosmetics.* 2020;7(4):77. [[CrossRef](#)].
79. Baptista A, Menicucci F, Brunetti C, Dos Santos Nascimento LB, Pasquini D, Alderotti F, et al. Unlocking the hidden potential of rosemary (*Salvia rosmarinus* Spenn.): New insights into phenolics, terpenes, and antioxidants of Mediterranean cultivars. *Plants.* 2024;13(23):3395. [[CrossRef](#)].
80. Böszörményi A, Dobi A, Skribanek A, Pávai M, Solymosi K. The effect of light on plastid differentiation, chlorophyll biosynthesis, and essential oil composition in rosemary (*Rosmarinus officinalis*) leaves and cotyledons. *Front Plant Sci.* 2020;11:196. [[CrossRef](#)].
81. Yosr Z, Hnia C, Rim T, Mohamed B. Changes in essential oil composition and phenolic fraction in *Rosmarinus officinalis* L. var. *typicus* Batt. organs during growth and incidence on the antioxidant activity. *Ind Crops Prod.* 2013;43:412–9. [[CrossRef](#)].
82. Houzi G, El abdali Y, Beniaich G, Chebaibi M, Taibi M, Elbouzidi A, et al. Antifungal, insecticidal, and repellent activities of *Rosmarinus officinalis* essential oil and molecular docking of its constituents against acetylcholinesterase and β -tubulin. *Scientifica.* 2024;2024:5558041. [[CrossRef](#)].
83. Rafya M, Zehhar N, Hafidi A, Benkhalti F. Review of *Rosmarinus officinalis* L. essential oil, hydrosol, and residues analysis: Composition, bioactivities, and valorization. *Ind Crops Prod.* 2024;221:119392. [[CrossRef](#)].
84. Andrade JM, Faustino C, Garcia C, Ladeiras D, Reis CP, Rijo P. *Rosmarinus officinalis* L.: An update review of its phytochemistry and biological activity. *Future Sci OA.* 2018;4(4):FSO283. [[CrossRef](#)].
85. Pandur E, Micalizzi G, Mondello L, Horváth A, Sipos K, Horváth G. Antioxidant and anti-inflammatory effects of thyme (*Thymus vulgaris* L.) essential oils prepared at different plant phenophases on *Pseudomonas aeruginosa* LPS-activated THP-1 macrophages. *Antioxidants.* 2022;11(7):1330. [[CrossRef](#)].
86. Aziz S, Habib-ur-Rehman, Irshad M, Asghar SF, Hussain H, Ahmed I. Phytotoxic and antifungal activities of essential oils of *Thymus serpyllum* grown in the state of Jammu and Kashmir. *J Essent Oil Bear Plants.* 2010;13(2):224–9. [[CrossRef](#)].

87. Kirillov V, Stikhareva T, Mukanov B, Chebotko N, Ryazantsev O, Atazhanova G, et al. Composition of the essential oil of *Thymus serpyllum* L. from northern Kazakhstan. J Essent Oil Bear Plants. 2016;19(1):212–22. [CrossRef].
88. Ellithy MM, Tarek HE, Saleh AM, El Azab EF, Ibrahim MN. Carvacrol as a promising topical agent against DMBA-induced oral cancer in rats: *In vivo* study. Pak J Biol Sci. 2025;28(9):576–86. [CrossRef].
89. Zhang T, Zheng Y, Fu C, Yang H, Liu X, Qiu F, et al. Chemical variation and environmental influence on essential oil of *Cinnamomum camphora*. Molecules. 2023;28(3):973. [CrossRef].
90. Yang XQ, Zheng H, Ye Q, Li RY, Chen Y. Essential oil of Cinnamon exerts anti-cancer activity against head and neck squamous cell carcinoma via attenuating epidermal growth factor receptor-tyrosine kinase. J BUON. 2015;20(6):1518–25.
91. Surducian DA, Racea RC, Cabuta M, Olariu I, Macasoi I, Rusu LC, et al. Eugenol induces apoptosis in tongue squamous carcinoma cells by mediating the expression of bcl-2 family. Life. 2022;13(1):22. [CrossRef].
92. Duan Y, Huang X, Qiao B, Ma R, Li J. Eugenol inhibits the biological activities of an oral squamous cell carcinoma cell line SCC9 via targeting MIF. Anticancer Agents Med Chem. 2022;22(15):2799–806. [CrossRef].
93. Issa H, Loubaki L, Al Amri A, Zibara K, Almutairi MH, Rouabhia M, et al. Eugenol as a potential adjuvant therapy for gingival squamous cell carcinoma. Sci Rep. 2024;14(1):10958. [CrossRef].
94. Jéssica SF, Ygor JR, de Queiroz George A, Elsie FG, André MM, Davyson DLM. *Piper rivinoides* Kunth: A medicinal plant that preserves bioactive chemical substances in its essential oil throughout the seasons. J Med Plants Res. 2022;16(8):258–68. [CrossRef].
95. Spréa RM, Fernandes Â, Finimundy TC, Pereira C, Alves MJ, Calhelha RC, et al. Lovage (*Levisticum officinale* W.D.J. Koch) roots: A source of bioactive compounds towards a circular economy. Resources. 2020;9(7):81. [CrossRef].
96. Miran M, Monsef Esfahani H, Moridi Farimani M, Ali Ahmadi A, Ebrahimi SN. Essential oil composition and antibacterial activity of *Levisticum officinale* Koch at different developmental stages. J Essent Oil Bear Plants. 2018;21(4):1051–5. [CrossRef].
97. Pasdaran A, Nahar L, Asnaashari S, Sarker SD, Delazar A. GC-MS analysis, free-radical-scavenging and insecticidal activities of essential oil of *Scrophularia oxysepala* Boiss. Pharm Sci. 2013;19(1):1–5.
98. Al-Dalameh Y, Almahmoud SAJ, Al-Bataineh N, Alghzawi TA, Alhamzani AG, Al-Mutairi AA, et al. *Scrophularia peyronii* post. from Jordan: Chemical composition of essential oil and phytochemical profiling of crude extracts and their *in vitro* antioxidant activity. Life. 2023;13(6):1404. [CrossRef].
99. Sertel S, Eichhorn T, Plinkert PK, Efferth T. Anticancer activity of *Salvia officinalis* essential oil against HNSCC cell line (UMSCC1). HNO. 2011;59(12):1203–8. [CrossRef].
100. Preusche M, Vahl M, Riediger J, Ulbrich A, Schulz M. Modulating expression levels of TCP transcription factors by *Mentha x piperita* volatiles—An allelopathic tool to influence leaf growth? Plants. 2022;11(22):3078. [CrossRef].
101. Öztürk Z, Bayar Muluk N, Keskin SU, Bulbul MV, Alaskarov E, Cingi C. Peppermint (*Mentha piperita*) essential oil induces dose-dependent cytotoxicity in human laryngeal carcinoma cells (HNO₂10). J Craniofac Surg. 2026;37(7–8):e607–12. [CrossRef].
102. Hu H, Li D, Bai R, Zhang W, Luo H, Yu E. Chemodiversity and bioactivity of the essential oils of *Juniperus* and implication for taxonomy. Int J Mol Sci. 2023;24(20):15203. [CrossRef].
103. Huang XF, Chang KF, Lee SC, Li CY, Liao HH, Hsieh MC, et al. Extract of *Juniperus indica bertol* synergizes with cisplatin to inhibit oral cancer cell growth via repression of cell cycle progression and activation of the caspase cascade. Molecules. 2020;25(12):2746. [CrossRef].
104. Wang W, Li N, Luo M, Zu Y, Efferth T. Antibacterial activity and anticancer activity of *Rosmarinus officinalis* L. essential oil compared to that of its main components. Molecules. 2012;17(3):2704–13. [CrossRef].
105. Rašković A, Milanović I, Pavlović N, Čebović T, Vukmirović S, Mikov M. Antioxidant activity of rosemary (*Rosmarinus officinalis* L.) essential oil and its hepatoprotective potential. BMC Complement Altern Med. 2014;14(1):225. [CrossRef].
106. Swamy MK, Akhtar MS, Sinniah UR. Antimicrobial properties of plant essential oils against human pathogens and their mode of action: An updated review. Evid Based Complement Alternat Med. 2016;2016:3012462. [CrossRef].
107. Imam MW, Luqman S. Unveiling the mechanism of essential oil action against skin pathogens: From ancient wisdom to modern science. Arch Microbiol. 2024;206(8):347. [CrossRef].

108. Bullaro V, Martinelli F, Lounès-Hadj Sahraoui A, Oufensou S. Molecular responses of phytopathogenic fungi to essential oil application: Current knowledge and perspectives. *Physiol Mol Plant Pathol.* 2025;140:102974. [[CrossRef](#)].
109. Pavan B, Bianchi A, Botti G, Ferraro L, Valerii MC, Spisni E, et al. Pharmacokinetic and permeation studies in rat brain of natural compounds led to investigate eugenol as direct activator of dopamine release in PC12 cells. *Int J Mol Sci.* 2023;24(2):1800. [[CrossRef](#)].
110. Nagoor Meeran MF, Javed H, Al Taei H, Azimullah S, Ojha SK. Pharmacological properties and molecular mechanisms of thymol: Prospects for its therapeutic potential and pharmaceutical development. *Front Pharmacol.* 2017;8:380. [[CrossRef](#)].
111. Latorre R, Valerii MC, Benati M, Lewis RE, Spigarelli R, Bernacchi A, et al. Lights and shadows of essential oil-derived compounds: Antimicrobial and anti-inflammatory properties of eugenol, thymol, cinnamaldehyde, and carvacrol. *Curr Issues Mol Biol.* 2025;47(11):915. [[CrossRef](#)].